Progresif Pulmoner Fibrozis
Klinik ve Fonksiyonel Değerlendirme

Dr. Nuri Tutar

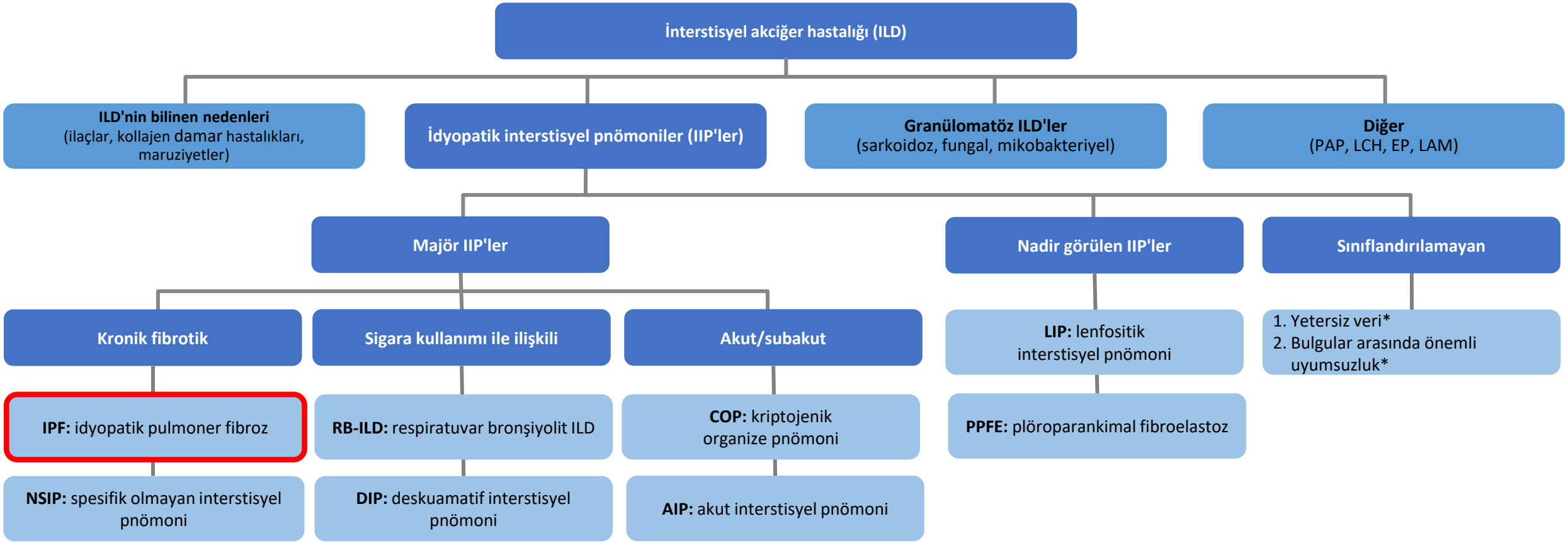
Erciyes Üniversitesi Tıp Fakültesi Göğüs Hastalıkları AD

Giriş

- İnterstisyel akciğer hastalıkları, fibrozisle karakterize büyük bir hastalık grubunu ifade etmektedir. Prevelansı ABD de **74/100.000** ve Avrupa'da **76/100.000** dir.
- İPF ise her zaman **progresif** olan ve **en sık** görülen intestisyel akciğer hastalığıdır.

Olson AL, Eur Respir Rev 2018; 27.

Sınıflama



Uyarlandığı kaynak: American Thoracic Society/European Respiratory Society; Am J Respir Crit Care Med 2002;165:277–304; Ryerson CJ, et al. Curr Opin Pulm Med **2013**;19:453–459; Travis WD, et al. Am J Respir Crit Care Med 2013;188:733–748.

İPF nin tanımlanması

Current Review

CMAJ, VOL. 137, DECEMBER 1, 1987

Idiopathic pulmonary fibrosis: a historical review

Jiri Homolka, MD, PhD

Hamman and Rich are generally considered to have been the first to describe idiopathic pulmonary fibrosis (IPF) as a new clinical and pathological entity. However, several earlier reports in the German-language literature described autopsy findings consistent with IPF from a contemporary point of view. The author discusses these and later reports in a review of the history, diagnosis and treatment of the disease.

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chronic changes he
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Hamman ve Rich 1933 ve 1944 yılarında İPF yi tanımlasa da farklı dillerdeki yayınlar incelendiğinde, ilk tanımlaması 1800 lü yılların sonu ve 1900 lü yıllarından başına varmaktadır.

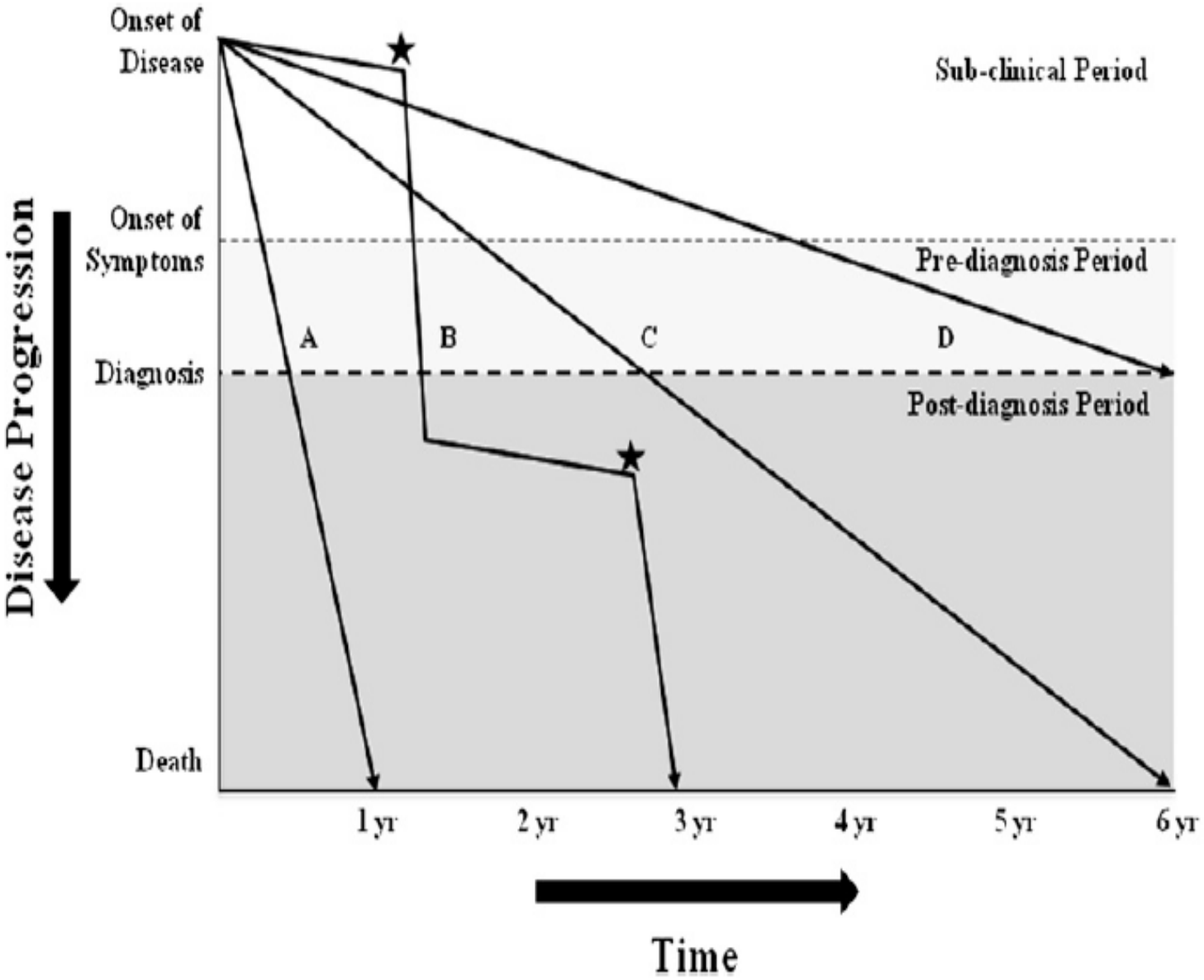


Figure 1. Schematic representation of potential clinical courses of idiopathic pulmonary fibrosis (IPF). As disease progresses, there is a subclinical period in which only radiographic findings of disease may be present, followed by a symptomatic period consisting of both pre-diagnosis and post-diagnosis clinical phases. The rate of decline and progression to death may be rapid (*line A*), slow (*lines C* and *D*), or mixed (*curve B*), with periods of relative stability interposed with periods of acute decline (*star*).

Prednisone, Azathioprine, and *N*-Acetylcysteine for Pulmonary Fibrosis

The Idiopathic Pulmonary Fibrosis Clinical Research Network*

N Engl J Med 2012;366:1968-77.

ABSTRACT

BACKGROUND

A combination of prednisone, azathioprine, and *N*-acetylcysteine (NAC) has been widely used as a treatment for idiopathic pulmonary fibrosis. The safety and efficacy of this three-drug regimen is unknown.

METHODS

In this randomized, double-blind, placebo-controlled trial, we assigned patients with idiopathic pulmonary fibrosis who had mild-to-moderate lung-function impairment to one of three groups — receiving a combination of prednisone, azathioprine, and NAC (combination therapy), NAC alone, or placebo — in a 1:1:1 ratio. The primary outcome was the change in longitudinal measurements of forced vital capacity during a 60-week treatment period.

RESULTS

When approximately 50% of data had been collected (with 77 patients in the combination-therapy group and 78 in the placebo group), a planned interim analysis revealed that patients in the combination-therapy group, as compared with the placebo group, had an increased rate of death (8 vs. 1, $P=0.01$) and hospitalization (23 vs. 7, $P<0.001$). These observations, coupled with no evidence of physiological or clinical benefit for combination therapy, prompted the independent data and safety monitoring board to recommend termination of the combination-therapy group at a mean follow-up of 32 weeks. Data from the ongoing comparison of the NAC-only group and the placebo group are not reported here.

CONCLUSIONS

Increased risks of death and hospitalization were observed in patients with idiopathic pulmonary fibrosis who were treated with a combination of prednisone, azathioprine, and NAC, as compared with placebo. These findings provide evidence against the use of this combination in such patients. (Funded by the National Heart, Lung, and Blood Institute and the Cowlin Family Fund; ClinicalTrials.gov number, NCT00650091.)

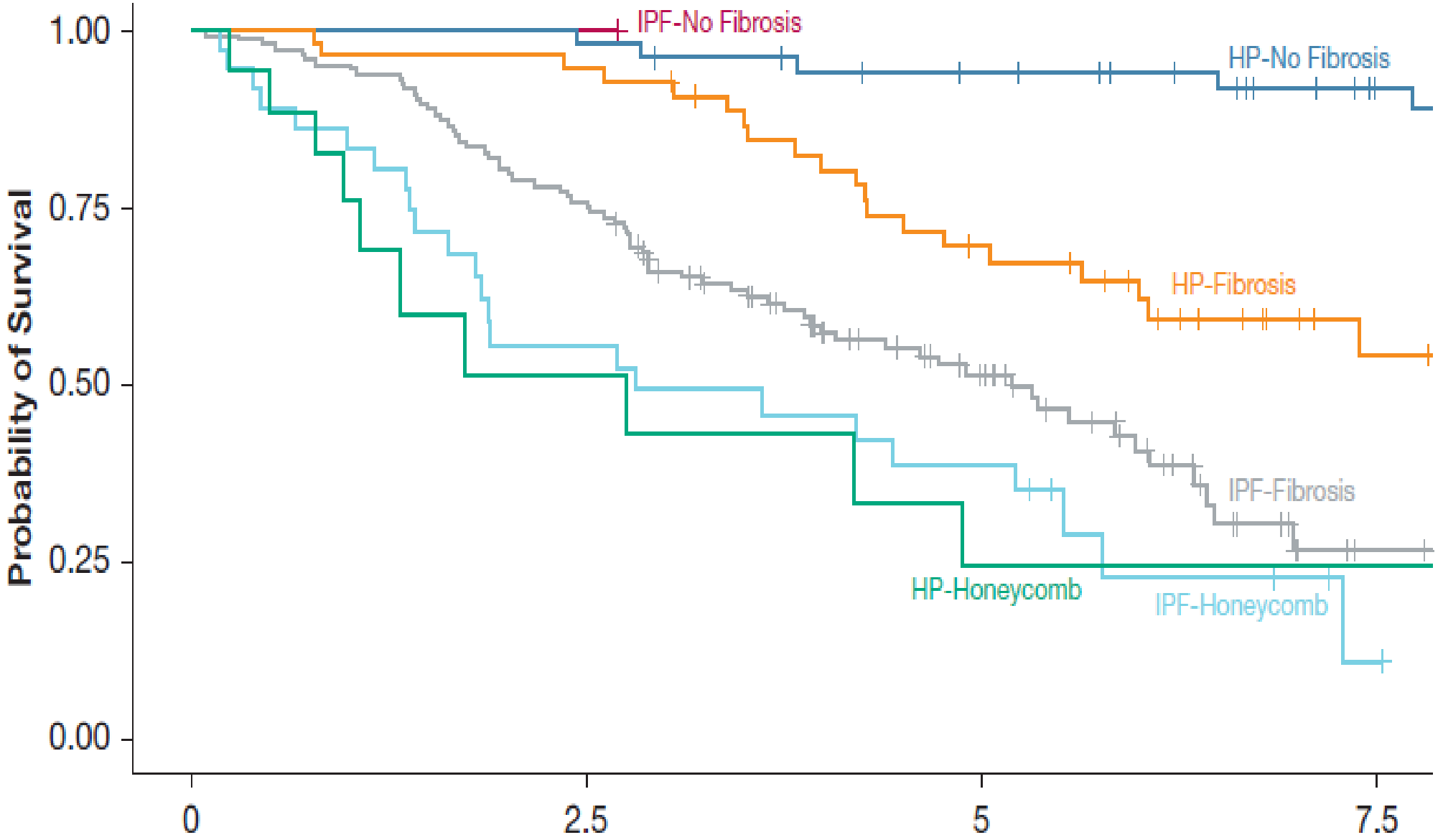
- İPF dışındaki bazı İAH alt tipleri de **ilerleyici fibrotik davranış** gösterebilir.
- Bu İAH'lar arasında etiyoloji farklı olsa da, **ortak patolojik mekanizmalar, klinik ve radyolojik bulgular** ve **prognoz** nedeniyle örtüşmeler mevcuttur.

Rajan KS, Eur Respir J 2023; 61: 2103187

› Chest. 2019 Apr;155(4):699-711. doi: 10.1016/j.chest.2018.08.1076. Epub 2018 Sep 19.

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

Margaret L Salisbury [1], Tian Gu [2], Susan Murray [2], Barry H Gross [3], Aamer Chughtai [3], Mohamed Sayyouh [3], Ella A Kazerooni [3], Jeffrey L Myers [4], Amir Lagstein [4], Kristine E Konopka [4], Elizabeth A Belloli [5], Jamie S Sheth [5], Eric S White [5], Colin Holtze [5], Fernando J Martinez [6], Kevin R Flaherty [5]

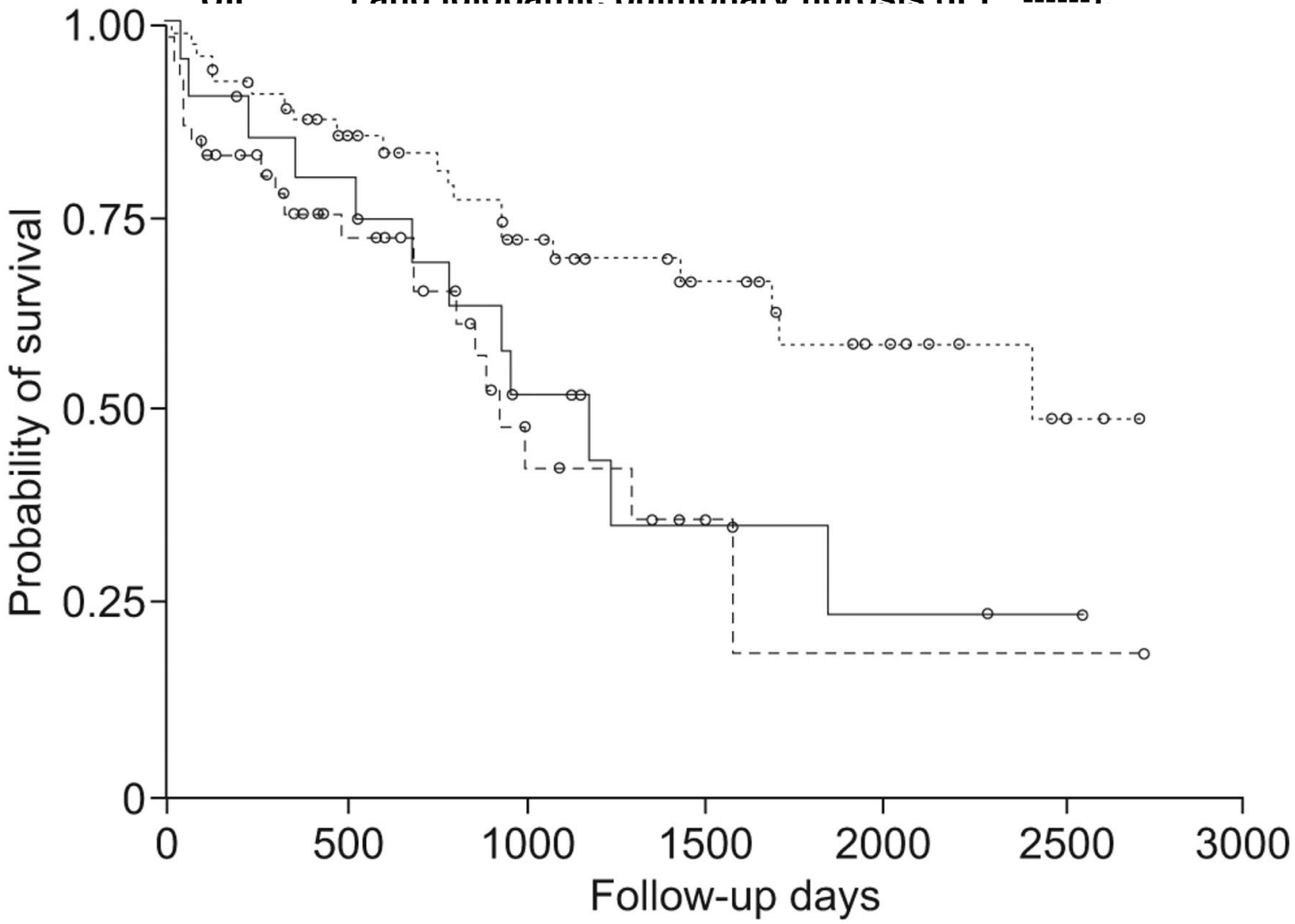

Probability of Survival
1.00
0.75
0.50
0.25
0.00
0
2.5
5
7.5
IPF-No Fibrosis
HP-No Fibrosis
HP-Fibrosis
IPF-Fibrosis
HP-Honeycomb
IPF-Honeycomb

Eur Respir J 2010; 35: 1322–1328
DOI: 10.1183/09031936.00092309

Usual interstitial pneumonia in rheumatoid arthritis-associated interstitial lung disease

E.J. Kim*, B.M. Elicker#, F. Maldonado¶, W.R. Webb#, J.H. Ryu¶, J.H. Van Uden#, J.S. Lee*, T.E. King Jr* and H.R. Collard*

Kaplan–Meier survival curve for patients with a rheumatoid arthritis (RA)-associated usual interstitial pneumonia (UIP) pattern (RA-UIP; ——), a RA-associated non-UIP pattern (RA-non-UIP; ……) and idiopathic pulmonary fibrosis (IPF; ------).



E. J. Kim et al. Eur Respir J 2010;35:1322-1328

Journal of
Clinical Medicine

MDPI

Article

Effects of Corticosteroid Treatment and Antigen Avoidance in a Large Hypersensitivity Pneumonitis Cohort: A Single-Centre Cohort Study

Laurens J. De Sadeleer [1,2,*], Frederik Hermans [1], Els De Dycker [1], Jonas Yserbyt [1], Johny A. Verschakelen [3], Eric K. Verbeken [4], Geert M. Verleden [1,2] and Wim A. Wuyts [1,2]

[1] Department of Respiratory Diseases, Unit for interstitial lung diseases, University Hospitals Leuven, Leuven B-3000, Belgium; frederik.hermans@yahoo.com (F.H.); els.dedycker@uzleuven.be (E.D.D.); jonas.yserbyt@uzleuven.be (J.Y.); geert.verleden@uzleuven.be (G.M.V.); wim.wuyts@uzleuven.be (W.A.W.)

J. Clin. Med. **2019**, *8*, 14; doi:10.3390/jcm8010014

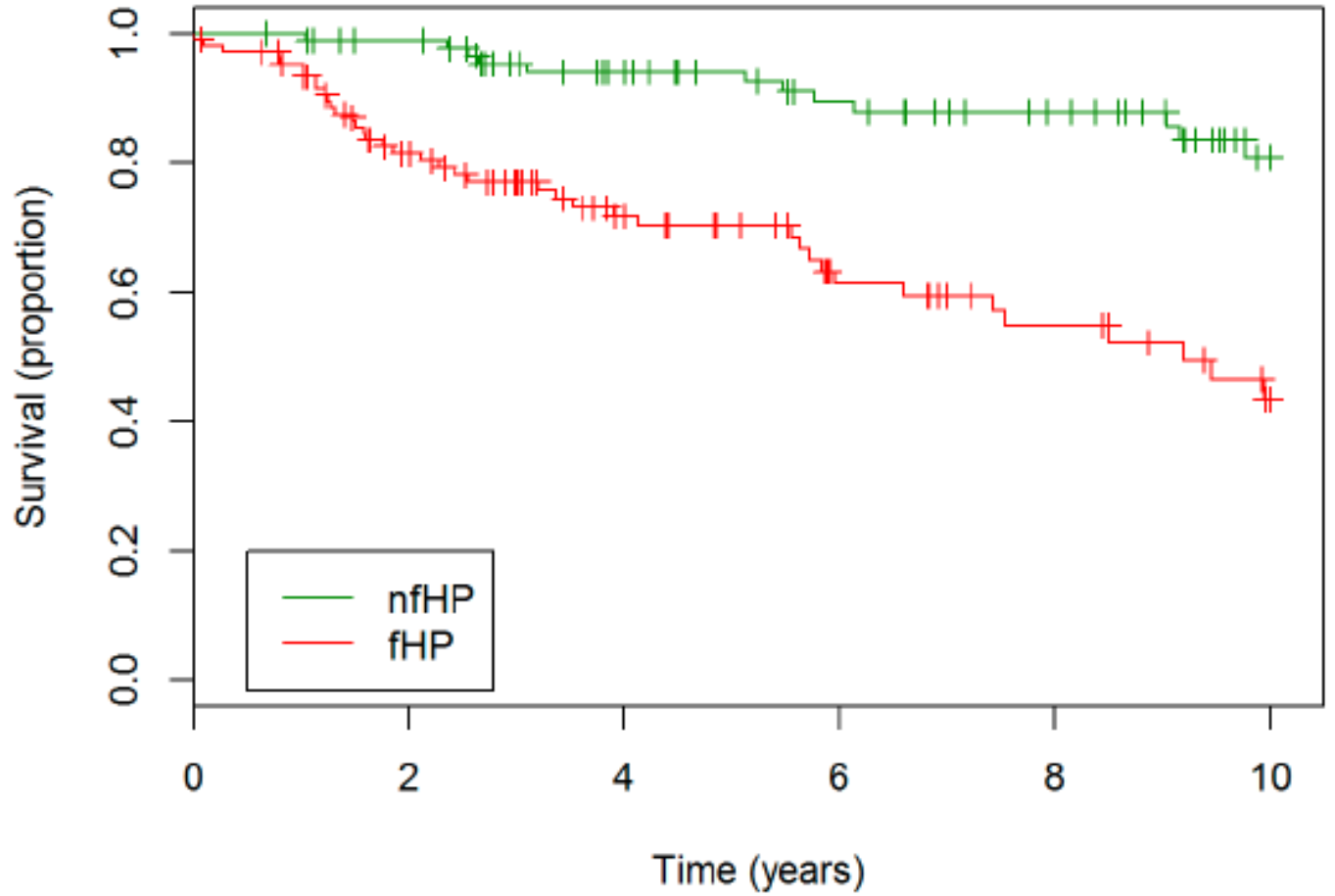
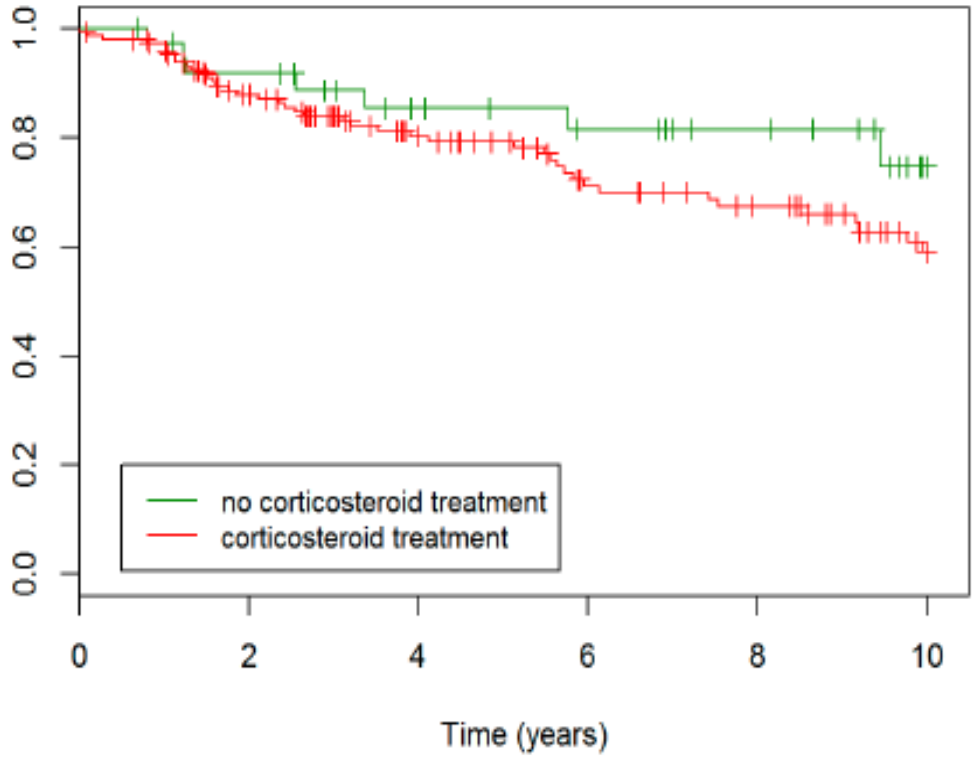
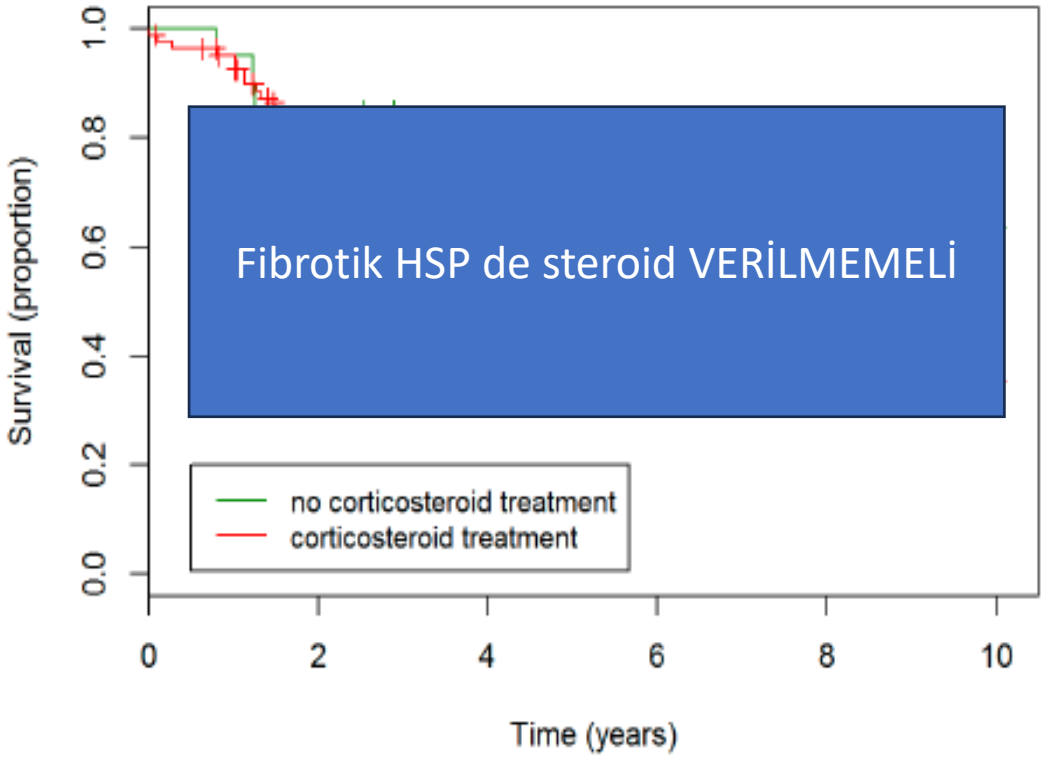


Figure 1. Survival nfHP and fHP patients. fHP patients experienced a worse outcome compared to nfHP patients. Definition of abbreviation: nfHP, non-fibrotic hypersensitivity pneumonitis, fHP, fibrotic chronic hypersensitivity pneumonitis

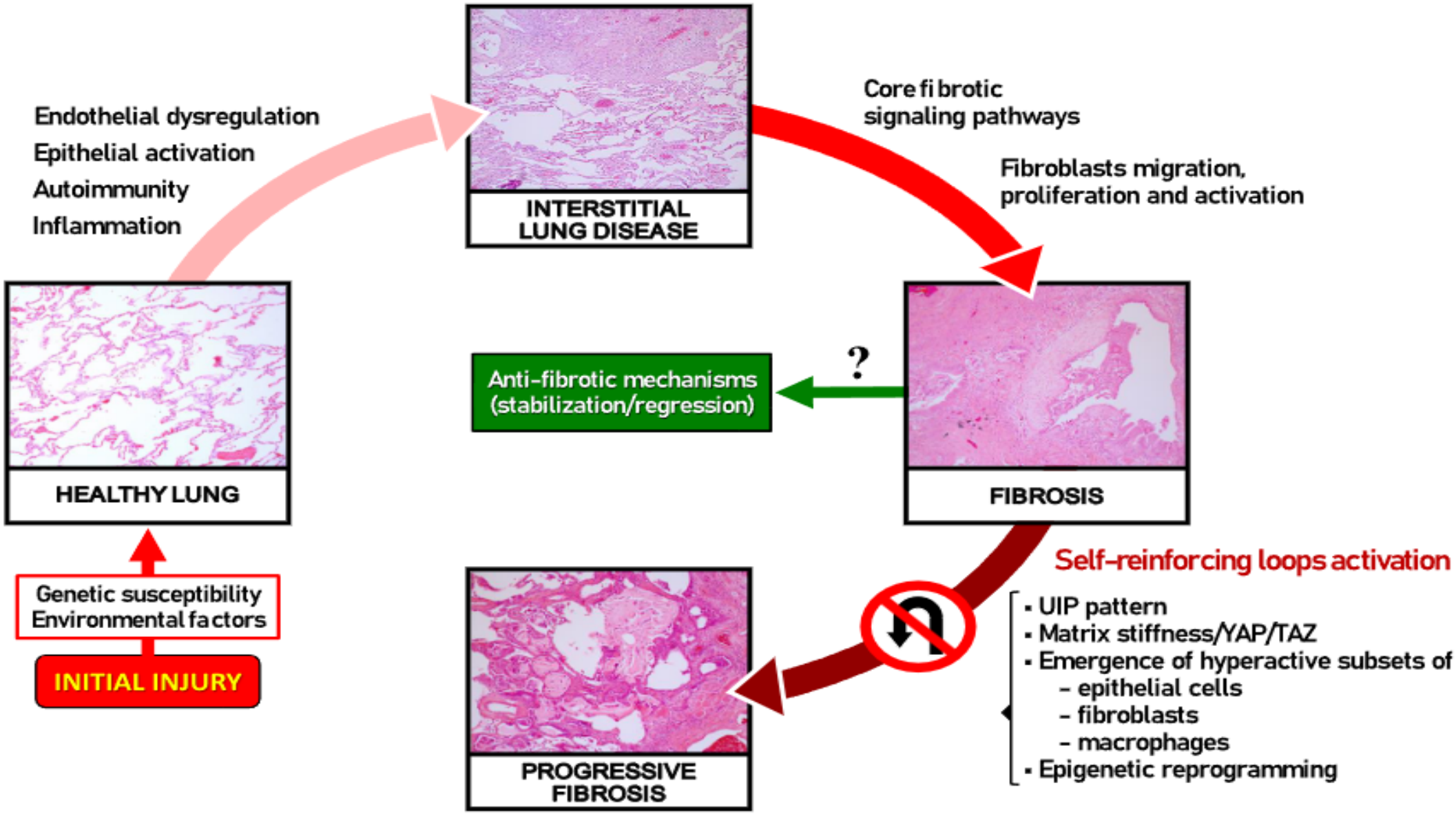


(a)



(b)

Figure 2. Survival in corticosteroid-treated patients compared to never-treated patients. (a) Kaplan Meier based on the entire cohort. No statistically significant differences were observed. (b) Kaplan Meier based on the fHP subgroup. A trend towards worse survival in the treated group was observed ($p = 0.096$).



Moises Selman, Am J Physiol Lung Cell Mol Physiol 321: L600–L607, 2021.

Progresyon kriterleri

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nintedanib in Progressive Fibrosing Interstitial Lung Diseases

K.R. Flaherty, A.U. Wells, V. Cottin, A. Devaraj, S.L.F. Walsh, Y. Inoue, L. Richeldi, M. Kolb, K. Tetzlaff, S. Stowasser, C. Coeck, E. Clerisme-Beaty, B. Rosenstock, M. Quaresma, T. Haeufel, R.-G. Goeldner, R. Schlenker-Herceg, and K.K. Brown, for the INBUILD Trial Investigators*

n engl j med 381;18 nejm.org October 31, 2019

INBUILD® : Önemli Dahil Edilme Kriterleri

- ≥18yaş
- Hekim tarafından tanı konmuş İPF dışı ILD
- Taramadan ≤12 ay önce yapılan ve merkezi incelemeyle doğrulanan

HRCT'de yaygınlık oranı >%10 olan diffüz fibrozan akciğer hastalığı özellikleri
(bal peteği görünümünün eşlik ettiği ya da etmediği traksiyon bronşektazisi bulunan retiküler anormallik)

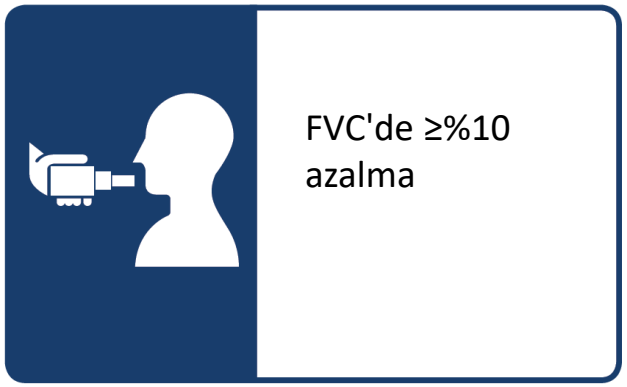
- FVC öngörülenin ≥%45'i
- DL_{CO} öngörülenin ≥%30-<%80'i

DL_{CO}, akciğerlerdeki karbon monoksit difüzyon kapasitesi; FVC, zorlu vital kapasite

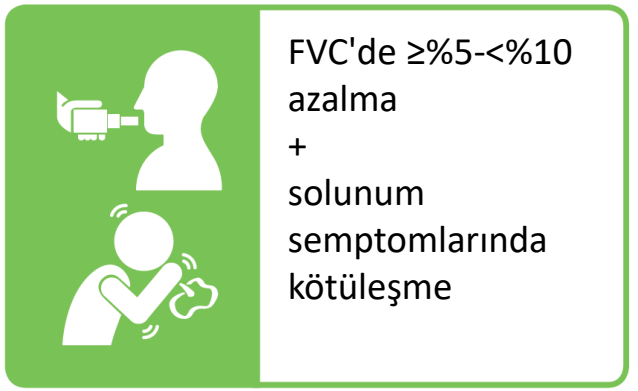
Flaherty KR et al. N Engl J Med 2019;381:1718-27.

INBUILD® : Progresyon Kriterleri

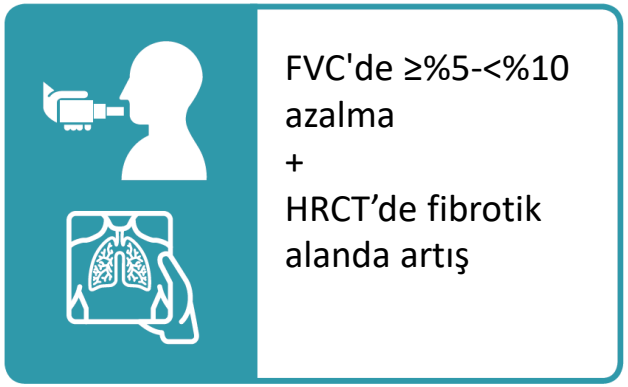
- Son 24 ay içerisinde standart hastalık yönetimine rağmen;



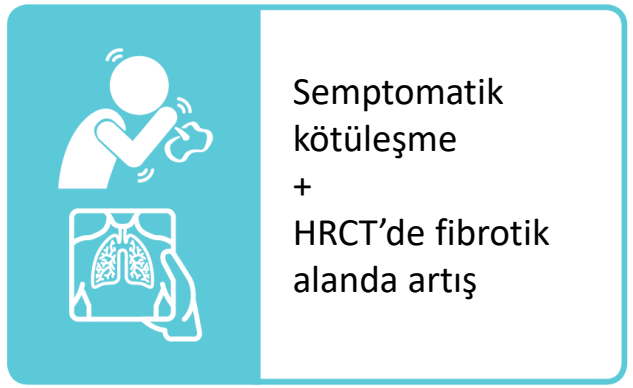
FVC'de ≥%10 azalma



FVC'de ≥%5-<%10 azalma
+
solunum semptomlarında kötüleşme



FVC'de ≥%5-<%10 azalma
+
HRCT'de fibrotik alanda artış



Semptomatik kötüleşme
+
HRCT'de fibrotik alanda artış

kriterler 24 ay süresince **herhangi bir noktada karşılanmıştır**, 24 ay bekleme şartı yoktur

Flaherty KR et al. N Engl J Med 2019;381:1718-27.

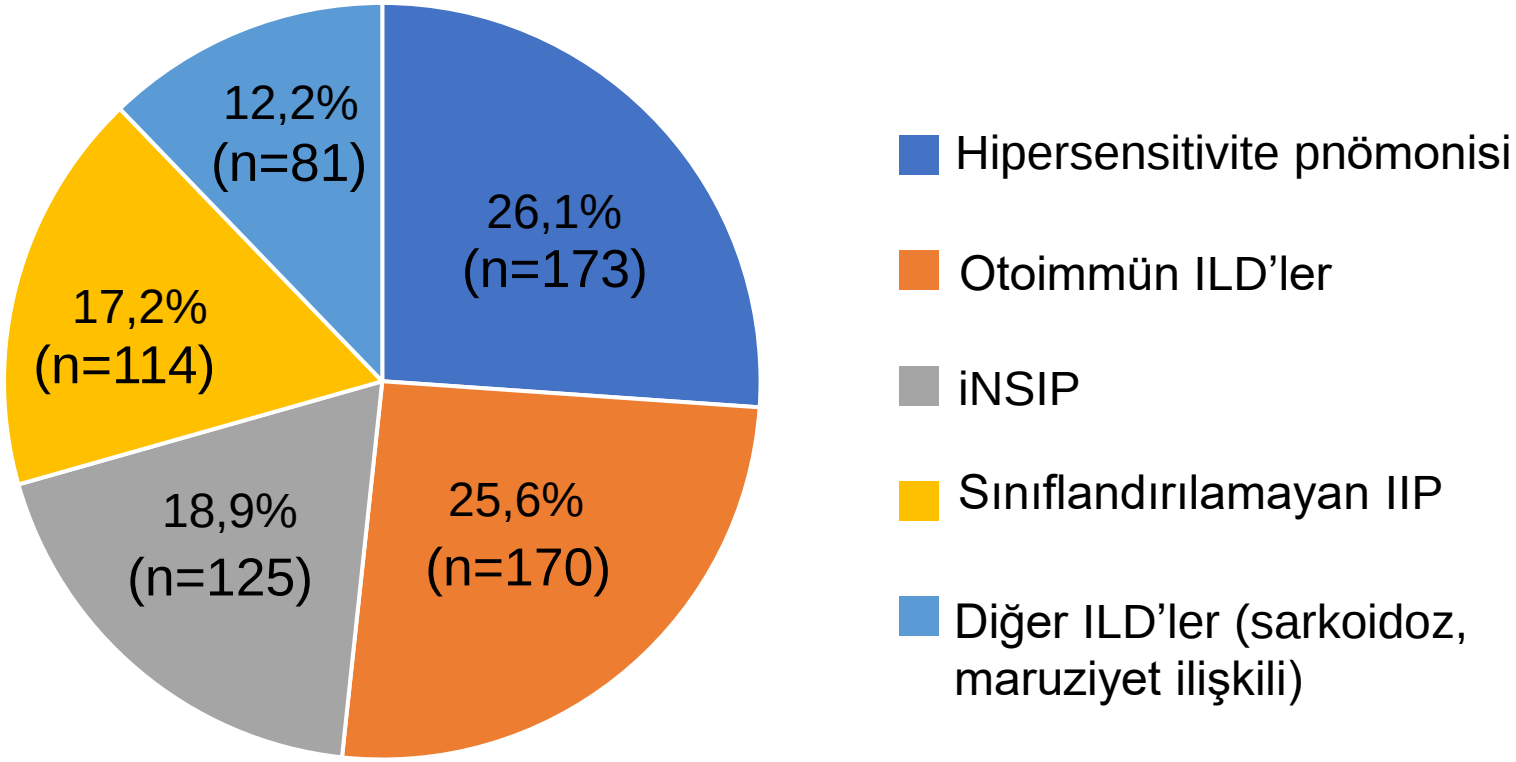
INBUILD® : Genel popülasyonun başlangıç özellikleri (1/2)

	Nintedanib (n=332)	Plasebo (n=331)
Yaş, yıl, ortalama (SD)	65.2 (9.7)	66.3 (9.8)
Erkek, n (%)	179 (53.9)	177 (53.5)
Halen ya da daha önce sigara kullanan, n (%)	169 (50.9)	169 (51.1)
HRCT'de UIP benzeri fibrozis paterni, n (%)	206 (62.0)	206 (62.2)
Son 24 ayda progresyon kriteri, n (%)	160 (48.2)	172 (52.0)
• FVC'de ≥%10 öng. Azalma		
• FVC'de %5-10 öng. azalma ve solunum fonksiyonlarında kötüleşme veya HRCT'de fibrozisin yaygınlık derecesinde artış	110 (33.1)	97 (29.3)
• Kötüleşen solunum semptomları ve HRCT'de fibrozisin yaygınlık derecesinde artış	62 (18.7)	61 (18.4)

HRCT, yüksek çözünürlüklü bilgisayarlı tomografi; UIP, usual interstisyel pnömoni

Flaherty KR et al. N Engl J Med 2019;381:1718-27.

INBUILD® : Tüm popülasyonda ILD tanısı koyulan hastalar (5 grup)



Otoimmün ILD'ler: RA-ILD, SSc-ILD, Miks Bağ Dokusu İlişkili ILD, ayrıca "Diğer Fibrozan ILD'ler' kategorisindeki otoimmün ILD'ler
Diğer ILD'ler: sarkoidoz, maruziyetle ilişkili ILD'ler ve diğer fibrozan ILD'lerdeki terimler
Wells AU et al. Lancet Respir Med 2020;8:453-460.

Pirfenidone in patients with progressive fibrotic interstitial lung diseases other than idiopathic pulmonary fibrosis (RELIEF): a double-blind, randomised, placebo-controlled, phase 2b trial

*Jürgen Behr, Antje Prasse, Michael Kreuter, Johannes Johow, Klaus F Rabe, Francesco Bonella, Reiner Bonnet, Christian Grohe, Matthias Held, Heinrike Wilkens, Peter Hammerl, Dirk Koschel, Stefan Blaas, Hubert Wirtz, Joachim H Ficker, Wolfgang Neumeister, Nicolas Schönfeld, Martin Claussen, Nikolaus Kneidinger, Marion Frankenberger, Simone Hummler, Nicolas Kahn, Silke Tello, Julia Freise, Tobias Welte, Petra Neuser, Andreas Günther, on behalf of the RELIEF investigators**

Lancet Respir Med 2021; 9: 476–86

Published Online March 30, 2021

Summary

Background Pirfenidone has been shown to slow disease progression in patients with idiopathic pulmonary fibrosis (IPF). However, there are few treatment options for progressive fibrotic interstitial lung diseases (ILDs)) other than IPF. In view of the pathomechanistic and clinical similarities between IPF and other progressive fibrotic ILDs, we aimed to assess the efficacy and safety of pirfenidone in patients with four non-IPF progressive fibrotic ILDs.

- Uygun katılımcılar dört tanıya bağlı ilerleyici fibrotik İAH olan 18-80 yaş arası hastalardı: kollajen veya vasküler hastalıklar (yani, bağ dokusu hastalığı ile ilişkili İAH'ler), fibrotik spesifik olmayan interstisyel pnömoni, kronik hipersensitivite pnömonisi veya asbest kaynaklı akciğer fibrozu.
- Diğer uygunluk kriterleri arasında zorlu vital kapasitenin (FVC) tahminen %40-90 olması, akciğerin karbon monoksit için difüzyon kapasitesinin tahminen %25-75 olması (sonrasında uygun hasta bulabilmek için 10-90 aralığına çekilmiş) ve **kayıttan önceki 6-24 ay içinde en az üç ölçüme dayalı olarak konvansiyonel tedaviye rağmen FVC'de tahminen yıllık en az %5 düşüş olması yer almıştır**.

PF-IAH>>>>>>PPF

- **Progresif fibrotik interstisyel akciğer hastalıkları (PF İAH)** kötüleşen semptomlar, akciğer fonksiyonlarında azalma, radyolojik progresyon, tedaviye zayıf yanıt, düşük yaşam kalitesi ile karakterizedir ve erken mortalite ile ilişkilidir.
- **İPF en sık görülen**, şiddetli idiyopatik interstisyel pnömonidir (İİP) ve PF-İAH'nin prototipi olarak kabul edilmektedir.

Dildar Duman, Tuberk Toraks 2022;70(4):375-381

PF-IAH>>>>>>PPF

- Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults: An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline 2022 , PF-IAH yerine **PPF** tanımının kullanılmasını önermiştir.

PPF tanı kriterleri

- İPF dışı bilinen veya bilinmeyen etyolojiye sahip ve radyolojik olarak fibrozisi olan bir hastada **son 1 yıl içinde** başka bir kanıt olmadan aşağıdaki bulgularda **2 sinin** olmasına PPF denilir.
- 1- Solunumsal semptomlarda kötüleşme
- 2- Fizyolojik bulgularda bozulma
  - Mutlak FVC değerinde %5 veya daha fazla düşüş
  - Hb e göre düzeltimiş mutlak DLCO değerinde %10 veya daha fazla düşüş

Raghu G, Am J Respir Crit Care Med, 2022, Vol 205, Iss 9, pp e18–e47

- 3- Radyolojik bulgularda progresyon
  - Traksiyon bronşektazisi ve bronşiyolektazinin yaygınlığı veya şiddetinde artış
  - Traksiyon bronşektazisi ile birlikte yeni buzlu cam opasitesi
  - Yeni ince retikülasyonlar
  - Retiküler anormalliğin artışı (yaygınlık veya kabalaşması)
  - Yeni veya artan bal peteği
  - Artmış lobar hacim kaybı

  - **TEK BAŞINA BUZLU CAM OPASİTESİ YOK**

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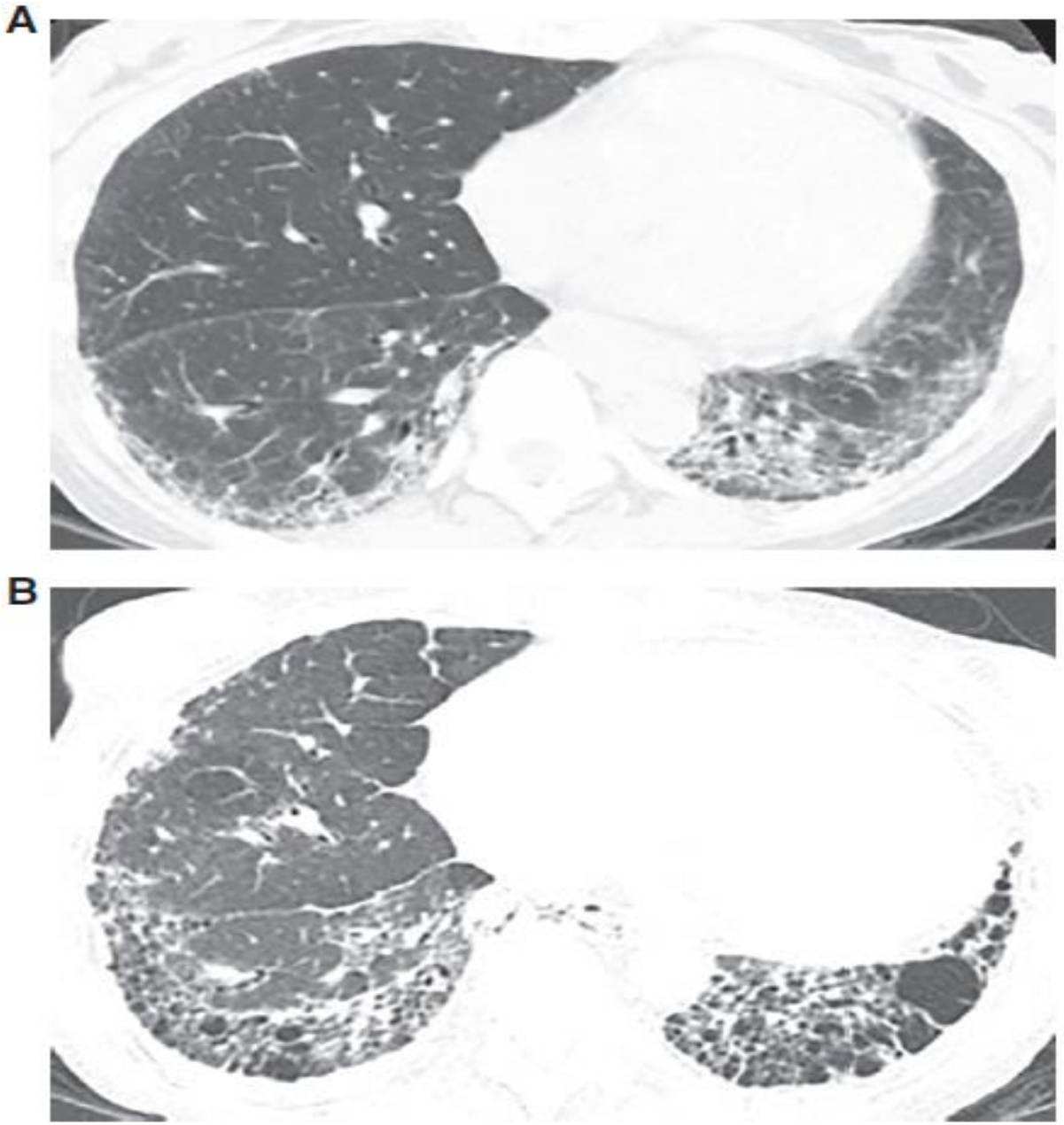

Figure 14. Progressive pulmonary fibrosis due to fibrotic nonspecific interstitial pneumonia (NSIP).

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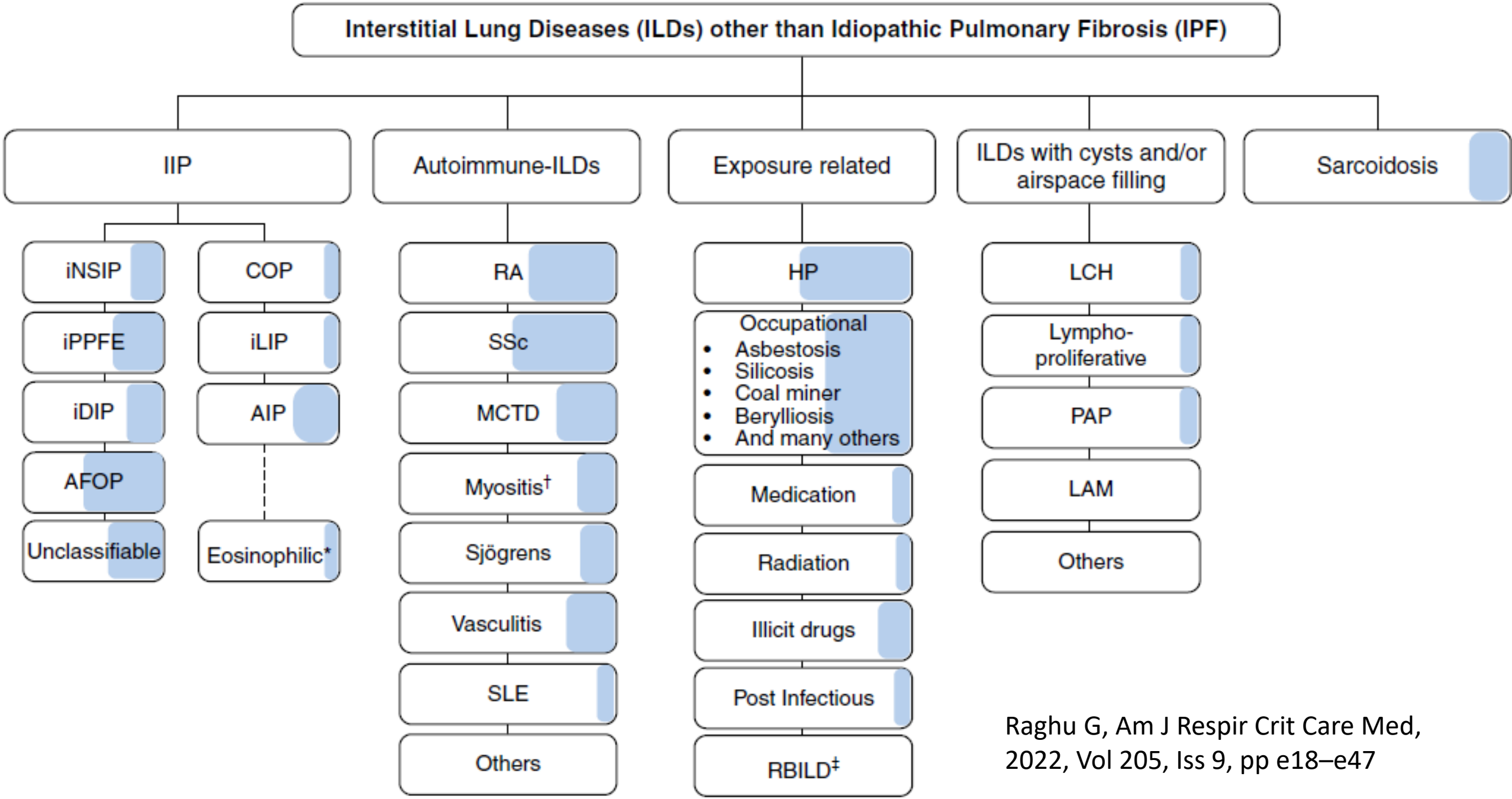
TABLE 1 Underlying common diagnoses of patients with fibrosing interstitial lung diseases (ILDs)
Idiopathic
Idiopathic interstitial pneumonia
Idiopathic non-specific interstitial pneumonia
Cryptogenic organising pneumonia with supervening fibrosis
Idiopathic desquamative interstitial pneumonia
Idiopathic lymphocytic interstitial pneumonia
Non-idiopathic
Connective tissue disease-ILDs
Fibrotic hypersensitivity pneumonitis
Exposure-related ILDs (asbestosis, silicosis, *etc.*)
Drug-induced ILDs (amiodarone, nitrofurantoin, *etc.*)
Sarcoidosis
Anti-neutrophilic cytoplasmic auto-antibody-associated vasculitis
Unclassifiable ILD
Although idiopathic pulmonary fibrosis is a progressive *and* fibrosing ILD, it is a separate, well-defined entity and has not been considered as part of potentially progressive pulmonary fibrosis for this statement.

Rajan KS, Eur Respir J 2023; 61: 2103187

İPF dışı İAH’larında progresyon oranı nedir?

- Komite tarafından göz önünde bulundurulan ek bir kriter de akut alevlenmedir, ancak kendi ayrı tanımı olduğu için PPF tanımı için uygun görülmemiştir.
- İAH'nin **akut alevlenmeleri** klasik olarak semptomatik ve görüntüleme değişikliklerine dayalı olarak tanımlanır ve yeni radyolojik anormallikler çoğunlukla genellikle inflamasyon veya akciğer hasarını temsil eden **buzlu cam opasiteleri** şeklinde görülür
- Uygulamada, klinisyenler alevlenmelerden sonra hastaları **yeniden değerlendirmeli** ve ilerlemenin meydana gelip gelmediğini belirlemek için bu değerlendirmeleri kullanmalıdır.

Raghu G, Am J Respir Crit Care Med, 2022, Vol 205, Iss 9, pp e18–e47



Raghu G, Am J Respir Crit Care Med, 2022, Vol 205, Iss 9, pp e18–e47

Progresyon oranı

- 3 klinik çalışma,
- Farklı progresyon kriterleri
- 473 İPF dışı interstisyel akciğer hastalıklarında 61-80 aylık sürede %18-32 sinin progrese olduğunu göstermiştir.
- **Fibrotik** interstisyel akciğer hastalıklarında ise oran **%13-40** dır.

Rajan KS, Eur Respir J 2023; 61: 2103187

Official Journal of the Asian Pacific Society of Respirology
Respirology

Original Article

Prevalence and prognosis of chronic fibrosing interstitial lung diseases with a progressive phenotype

Reoto Takei, Kevin K. Brown, Yasuhiko Yamano, Kensuke Kataoka, Toshiki Yokoyama, Toshiaki Matsuda, Tomoki Kimura, Atsushi Suzuki, Taiki Furukawa, Junya Fukuoka, Takeshi Johkoh ... See all authors

First published: 15 March 2022 | https://doi.org/10.1111/resp.14245 | Citations: 10

844 hasta
397 İPF
447 non-İPF FILD
Progresyon kriteri
FVC de %10 azalma
FVC de %5-9 azalma ve DLCO da %15 azalma, YÇBT de ilerleme veya semptom artışı

- İPF hastalarının **%59.4** ü, non-İPF FILD hastalarının **%26.6** sı progresyon gösteriyor (24 aylık takip)
- Progresyon fenotipine sahip İPF hastaları ve non-İPF FILD hastalarında progresyon olmayanlara göre transplantasyon olmadan yaşam süresi anlamlı şekilde düşük ($p<0.01$)
- Multiple variable analize göre progresyon mortalite için bağımsız değişken (hazard ratio [HR]: 3.36, 95% CI: 2.68–4.23, $p<0.01$).
- **Progresif İPF ve pogresif non-İPF FILD hastalarında mortalite benzer (p= 0.42)**

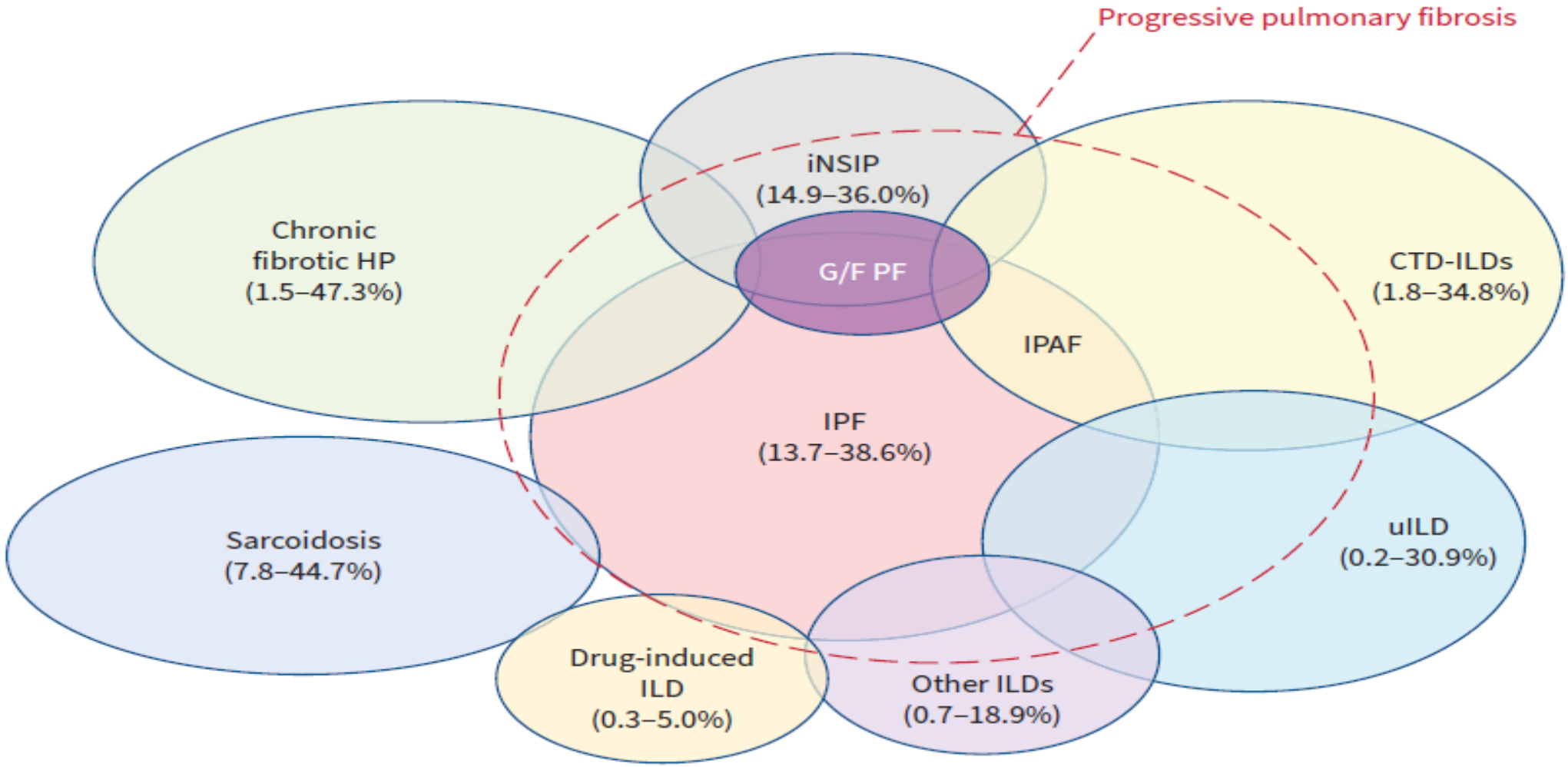


FIGURE 1 Schematic representation of the prevalent spectrum of interstitial lung diseases (ILDs) that may be associated with "progressive pulmonary fibrosis (despite management)". The lowest and highest prevalences across different countries are shown in brackets [14]. CTD: connective tissue disease; G/F PF: genetic and/or

Rajan KS, Eur Respir J 2023; 61: 2103187

Progresyon kriterleri ve mortalite

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ORIGINAL ARTICLE

Validation of Proposed Criteria for Progressive Pulmonary Fibrosis

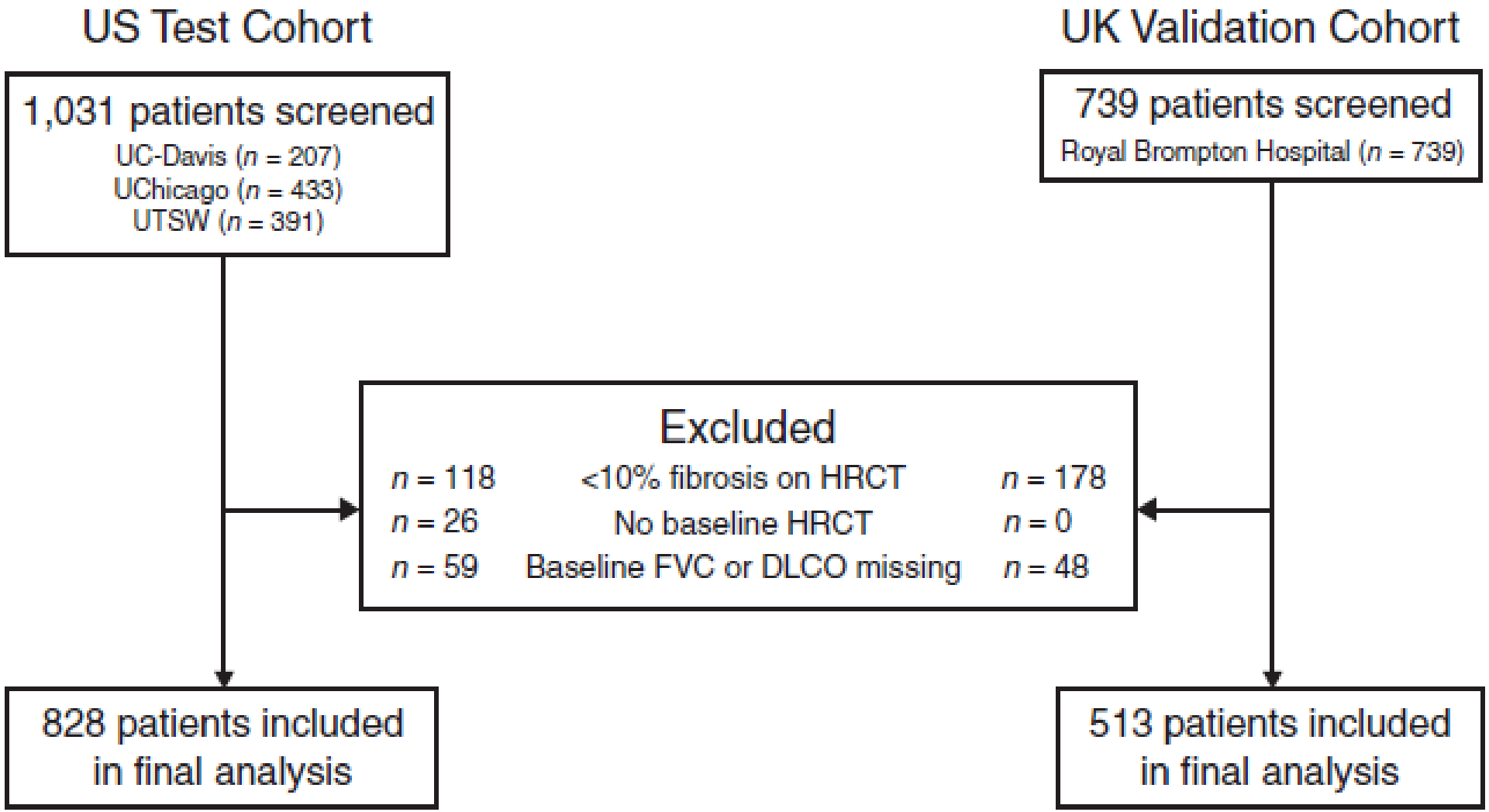
Janelle Vu Pugashetti[1,2*], Ayodeji Adegunsoye[3*], Zhe Wu[4,5], Cathryn T. Lee[3], Anand Srikrishnan[6], Sahand Ghodrati[2], Vivian Vo[2], Elisabetta A. Renzoni[4,5], Athol U. Wells[4,5], Christine Kim Garcia[7], Felix Chua[4,5], Chad A. Newton[6‡], Philip L. Molyneaux[4,5‡], and Justin M. Oldham[1‡]

[1]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan; [2]Division of Pulmonary, Critical Care and Sleep Medicine, University of California, Davis, Davis, California; [3]Section of Pulmonary and Critical Care Medicine, University of Chicago, Chicago, Illinois; [4]National Heart and Lung Institute, Imperial College London, London, United Kingdom; [5]Royal Brompton and Harefield Hospitals, Guy's and St. Thomas' NHS Foundation Trust, London, United Kingdom; [6]Division of Pulmonary and Critical Care Medicine, University of Texas Southwestern Medical Center, Dallas, Texas; and [7]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Columbia University, New York, New York

ORCID IDs: 0000-0002-8889-2757 (J.V.P.); 0000-0002-0771-1249 (C.K.G.); 0000-0003-4957-8869 (J.M.O.).

- Gerekçe: Progresif pulmoner fibrozis (PPF) için kriterler önerilmiştir, ancak bunların prognostik değeri ve FVC'deki kategorik düşüş belirsizliğini korumaktadır.
- Amaçlar: **Önerilen PPF kriterlerinin hastalarda nakilsiz sağkalımı (TFS) öngörmesi.**
- Yöntemler: Retrospektif, çok merkezli bir kohort analizi gerçekleştirildi. Fibrotik bağ dokusu tanısı olan hastalar hastalığa bağlı İAH, fibrotik hipersensitivite pnömonisi ve **ABD'deki üç merkezden** İPF dışı idiyopatik interstisyel pnömoni ve bir **Birleşik Krallık merkezi** kohortu oluşturmuştur**. 5 yıllık TFS ile >%10 FVC düşüşü arasındaki ilişki, ardından >%10 FVC düşüşü yoksa 13 ek PPF kriterinin karşılanması gerekmekte idi.**

1. A 5–9% relative FVC decline (stand-alone component of combined criteria below)
2. A 5–9% absolute FVC decline (6, 7)
3. A ⩾10% absolute D_{LCO} decline (stand-alone component of combined criteria below)
4. A ⩾15% relative D_{LCO} decline (9)
5. CT progression of fibrosis (stand-alone component of combined criteria below)
6. A 5–9% relative FVC decline and worsening respiratory symptoms (5, 8)
7. A 5–9% absolute FVC decline and worsening respiratory symptoms (10)
8. A 5–9% relative FVC decline and ⩾15% relative D_{LCO} decline (8)
9. A ⩾10% absolute D_{LCO} decline and worsening respiratory symptoms (10)
10. CT progression of fibrosis and worsening respiratory symptoms (5, 8, 10)
11. CT progression of fibrosis and 5–9% relative decline in FVC (5, 8, 9)
12. CT progression of fibrosis and 5–9% absolute FVC decline (10)
13. CT progression of fibrosis and ⩾10% absolute decline in D_{LCO} (10)


US Test Cohort
1,031 patients screened
UC-Davis (n = 207)
UChicago (n = 433)
UTSW (n = 391)
UK Validation Cohort
739 patients screened
Royal Brompton Hospital (n = 739)
Excluded
n = 118 <10% fibrosis on HRCT n = 178
n = 26 No baseline HRCT n = 0
n = 59 Baseline FVC or DLCO missing n = 48
828 patients included in final analysis
513 patients included in final analysis

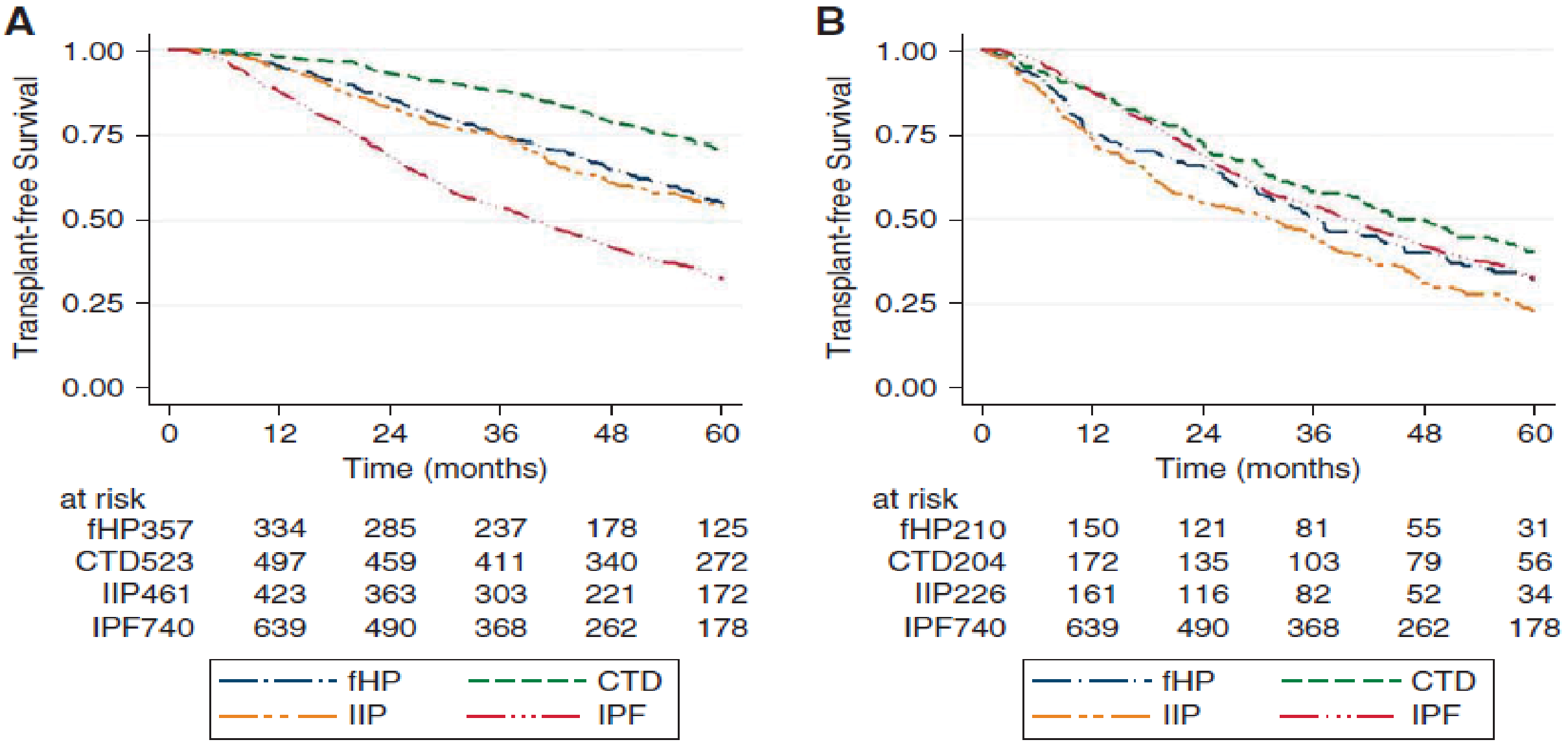
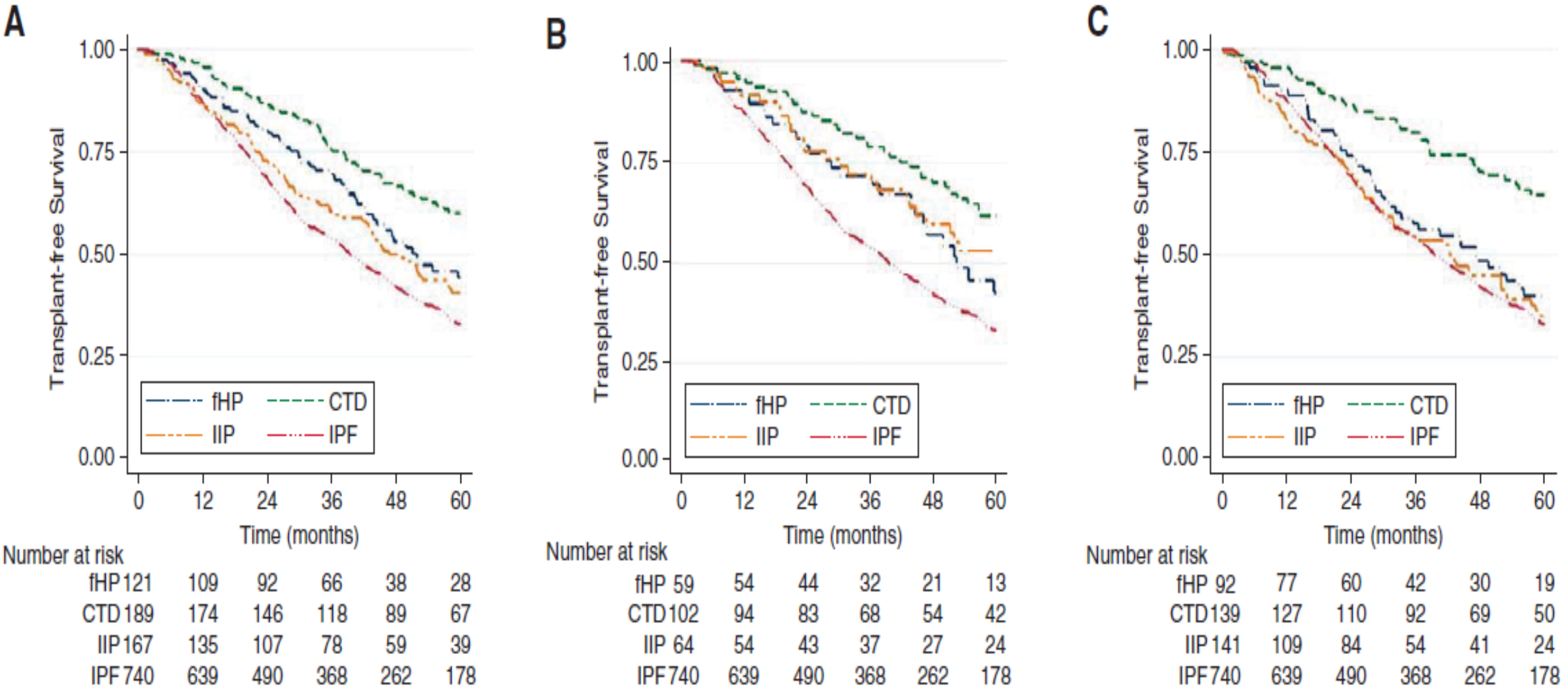
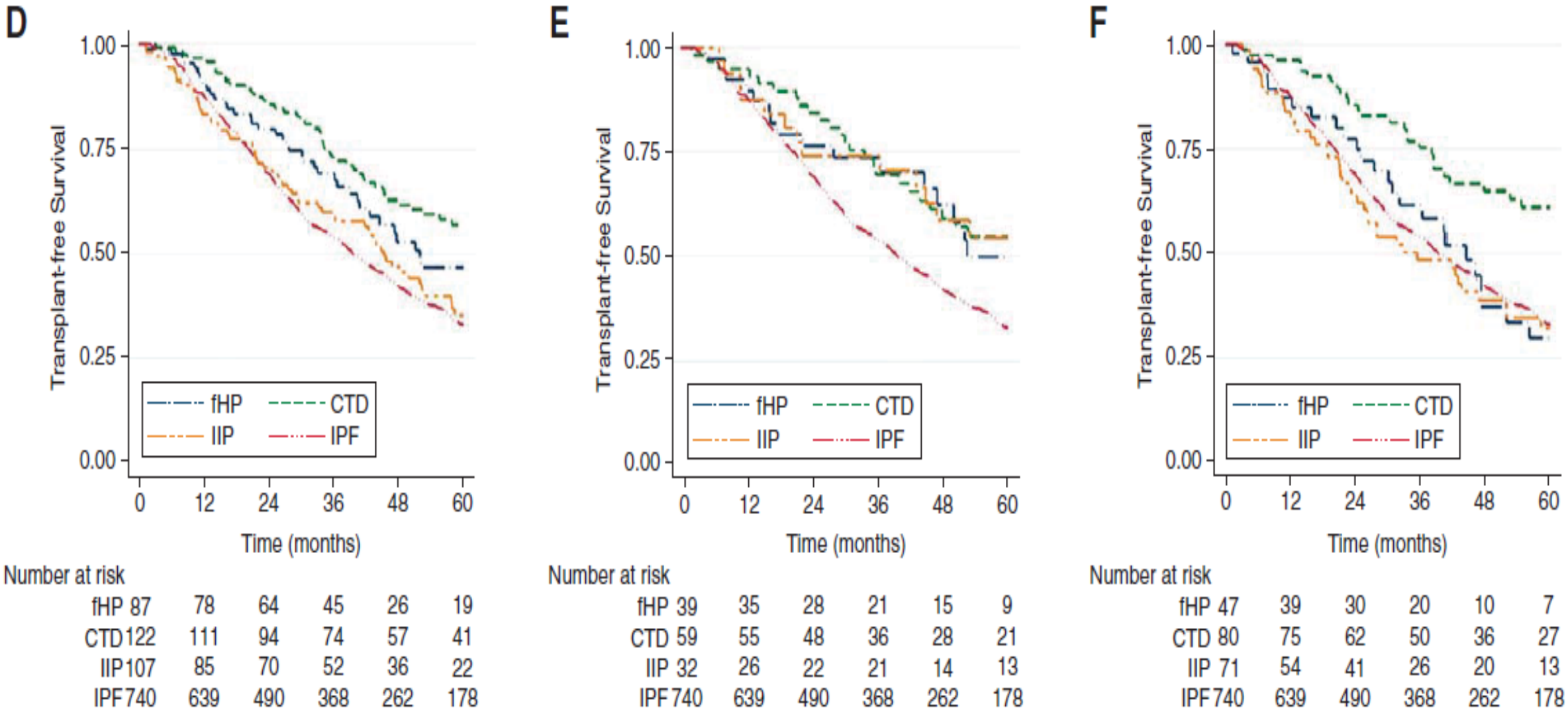


Figure 3. TFS among ILD subtypes. Although favorable compared with idiopathic pulmonary fibrosis (IPF) following diagnosis (*A*), TFS among fibrotic hypersensitivity pneumonitis, CTD-ILD, and non-IPF IIP closely approximated IPF after ⩾10% relative FVC decline (*B*).



(A) 5–9% relative FVC decline, (B) >15% relative DLCO decline, (C) CT progression of fibrosis,



(D) 5–9% relative FVC decline and worsening respiratory symptoms, (E) 5–9% relative FVC decline and >15% relative DLCO decline, and (F) CT progression of fibrosis and worsening respiratory symptoms

Table 2. Risk of Death or Lung Transplantation after Satisfying Proposed Progressive Pulmonary Fibrosis Criteria in U.S. Test and UK Validation Cohorts

PPF Criterion	U.S. Cohort (*n* = 828)			UK Cohort (*n* = 513)				Combined Cohort
	n	HR (95% CI)	*P* Value	*n*	HR (95% CI)	*P* Value	*P* Value*	HR (95% CI)
≥10% relative FVC decline	404/828	3.11 (2.37–4.08)	<0.001	241/513	3.34 (2.35–4.73)	<0.001	0.702	3.11 (2.51–3.85)
Excluding those with concurrent ≥10% relative FVC decline								
5–9% relative FVC decline	291/577	2.87 (2.04–4.03)	<0.001	183/366	2.36 (1.53–3.63)	<0.001	0.428	2.58 (1.98–3.35)
5–9% absolute FVC decline	146/535	2.50 (1.70–3.68)	<0.001	80/328	2.02 (1.22–3.33)	0.006	0.461	†
≥10% absolute D_{LCO} decline	203/624	1.93 (1.41–2.65)	<0.001	43/394	0.91 (0.45–1.81)	0.779	0.057	†
≥15% relative D_{LCO} decline	253/611	2.28 (1.65–3.13)	<0.001	116/366	2.19 (1.43–3.35)	<0.001	0.893	2.20 (1.71–2.83)
CT progression of fibrosis	135/524	1.81 (1.27–2.59)	0.001	62/324	2.43 (1.45–4.08)	0.001	0.577	1.99 (1.49–2.66)
5–9% relative FVC decline and worsening symptoms	190/574	2.68 (1.94–3.72)	<0.001	133/356	2.14 (1.41–3.27)	<0.001	0.420	2.42 (1.87–3.12)
5–9% absolute FVC decline and worsening symptoms	86/541	2.41 (1.58–3.67)	<0.001	44/323	1.89 (1.01–3.52)	0.046	0.542	†
5–9% relative FVC decline and ≥15% relative D_{LCO} decline	129/596	2.40 (1.70–3.40)	<0.001	67/368	2.29 (1.42–3.70)	<0.001	0.725	2.29 (1.73–3.02)
≥10% absolute D_{LCO} decline and worsening symptoms	126/648	1.85 (1.32–2.59)	<0.001	29/396	0.87 (0.37–2.00)	0.736	0.094	†
CT progression of fibrosis and worsening symptoms	93/525	2.26 (1.56–3.28)	<0.001	51/324	2.62 (1.54–4.48)	<0.001	0.961	2.32 (1.72–3.14)
CT progression of fibrosis and 5–9% relative FVC decline	50/493	1.63 (0.99–2.70)	0.055	25/302	1.33 (0.62–2.85)	0.467	0.402	†
CT progression of fibrosis and 5–9% absolute FVC decline	27/487	1.93 (1.01–3.71)	0.047	10/293	1.30 (0.38–4.39)	0.675	0.439	†
CT progression of fibrosis and ≥10% absolute D_{LCO} decline	35/486	2.13 (1.23–3.67)	0.007	9/288	1.00 (0.23–4.29)	0.988	0.324	†

- %10 veya daha fazla FVC düşüşü dışında progresif İAH alt tipinden bağımsız 6 kriter mortalite ile ilişkili bulundu.
- Bunlar

1- %5-9 relatif FVC düşüşü

2- %15 veya daha fazla relatif DLCO düşüşü

3- CT bulgularında progresyon

4- %5-9 relatif FVC düşüşü ve semptomlarda kötüleşme

5- %10 veya daha fazla relatif DLCO düşüşü ve semptomlarda kötüleşme

6- CT bulgularında progresyon ve semptomlarda kötüleşme

Progresyon için risk faktörleri nelerdir?

- Non- İPF interstisyel akciğer hastalıklarında gruplara spesifik risk faktörleri progresyonu öngörmede kullanılabilir mi?

TABLE 2 Risk factors for the progression of non-idiopathic pulmonary fibrosis interstitial lung diseases (ILDs)

Risk factor	First author (year) [ref.]	Hazard ratio (95% CI)	p-value
General risk factors			
UIP	Flaherty (2019) [2]	1.53 (−0.68–3.74)	NA
BMI	Alakhras (2007) [19]	0.93 (0.89–0.97)	0.002
Oxygen desaturation during 6MWT#	Alfieri (2020) [20]	OR¶ 8.7 (4.42–17.3)	NA
Disease			
Fibrotic hypersensitivity pneumonitis	Gimenez (2018) [21]		
Decline in FVC by ⩾10%	Gimenez (2018) [21]	4.13 (1.96–8.70)	0.005
Lower baseline FVC %	Gimenez (2018) [21]	1.03 (1.01–1.05)	0.003
Antigen identification	Gimenez (2018) [21]	0.18 (0.04–0.77)	0.021
MUC5B^{+}/*TLD*$^{+}$ (gene variants)	Ley (2019) [22]	3.52 (1.87–6.62)	0.00009
Rheumatoid arthritis-ILD	Zamora-Legoff (2017) [9]		
UIP *versus* NSIP	Zamora-Legoff (2017) [9]	3.29 (1.28–8.41)	0.013
High levels of CCP antibody/anti-CCP2 titres^{+}	Khan (2021) [23]	1.05 (1.01–1.10)	0.01
Smoking, 30 pack-years	Kronzer (2021) [24]	OR¶ 6.06 (2.72–13.5)	NA
Fibrotic score on HRCT	Solomon (2016) [25]	1.02 (1.01–1.03)	0.0002
Extent of fibrosis on HRCT	Solomon (2016) [25]	1.12 (1.08–1.17)	<0.000006
Systemic sclerosis	Goh (2017) [26]		
Low baseline FVC <65% and low baseline D_{LCO} ⩽55%	Sánchez-Cano (2018) [27]; Hoffmann-Vold (2019) [28]	OR¶ 1.02 (1.01–1.03)	<0.001
Decline in D_{LCO} >15%	Le Gouellec (2017) [29]	2.03 (1.25–3.29)	<0.005
Decline in K_{CO} >10%	Goh (2017) [26]	2.35 (1.40–3.95)	<0.001
Fibrotic score on HRCT	Ibrahim (2020) [30]	2.52 (1.16–5.49)	0.02
Extent of fibrosis on HRCT (HRCT extent 10–30% and FVC <70%)	Goh (2008) [31]	3.46 (2.19–5.46)	<0.0005

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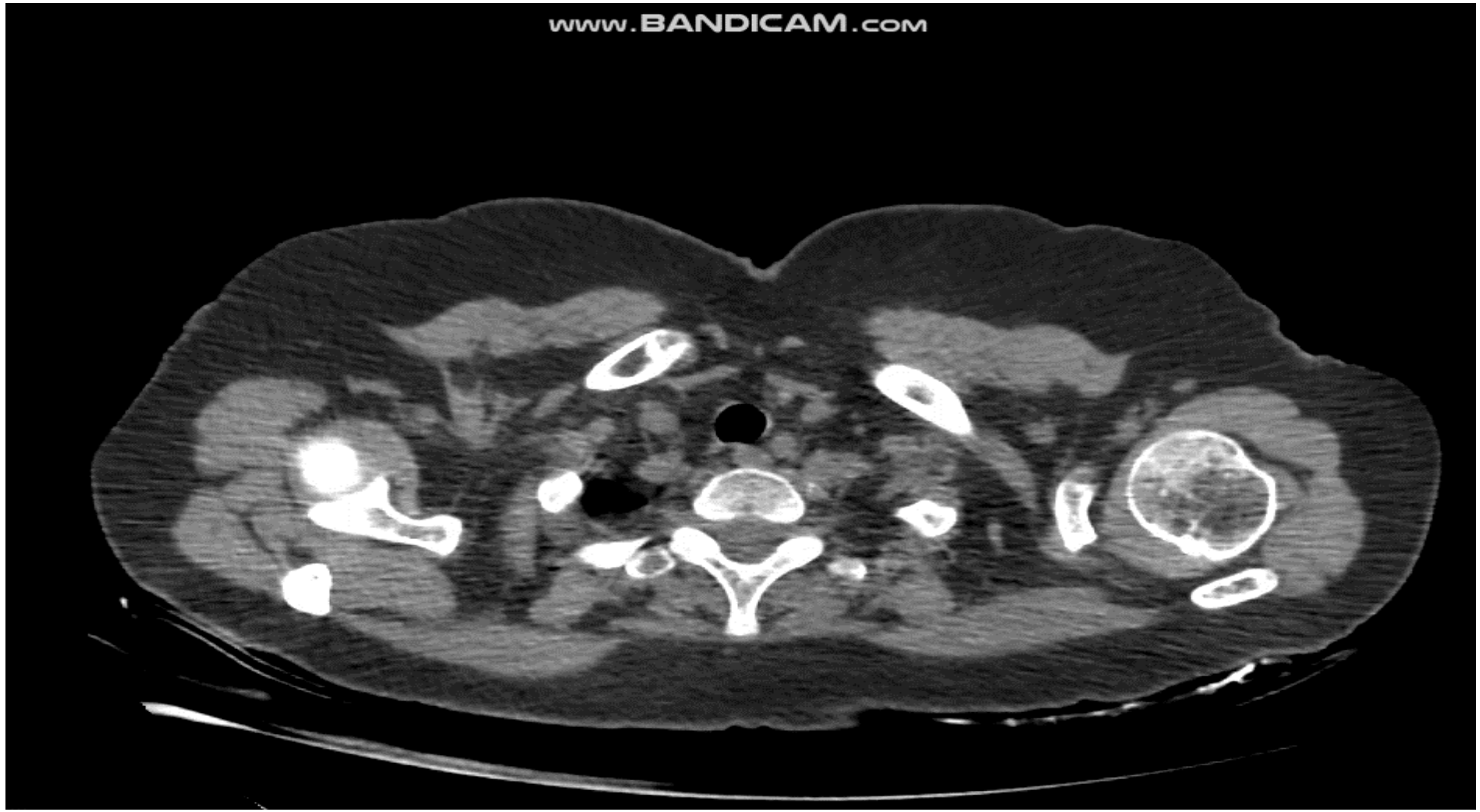
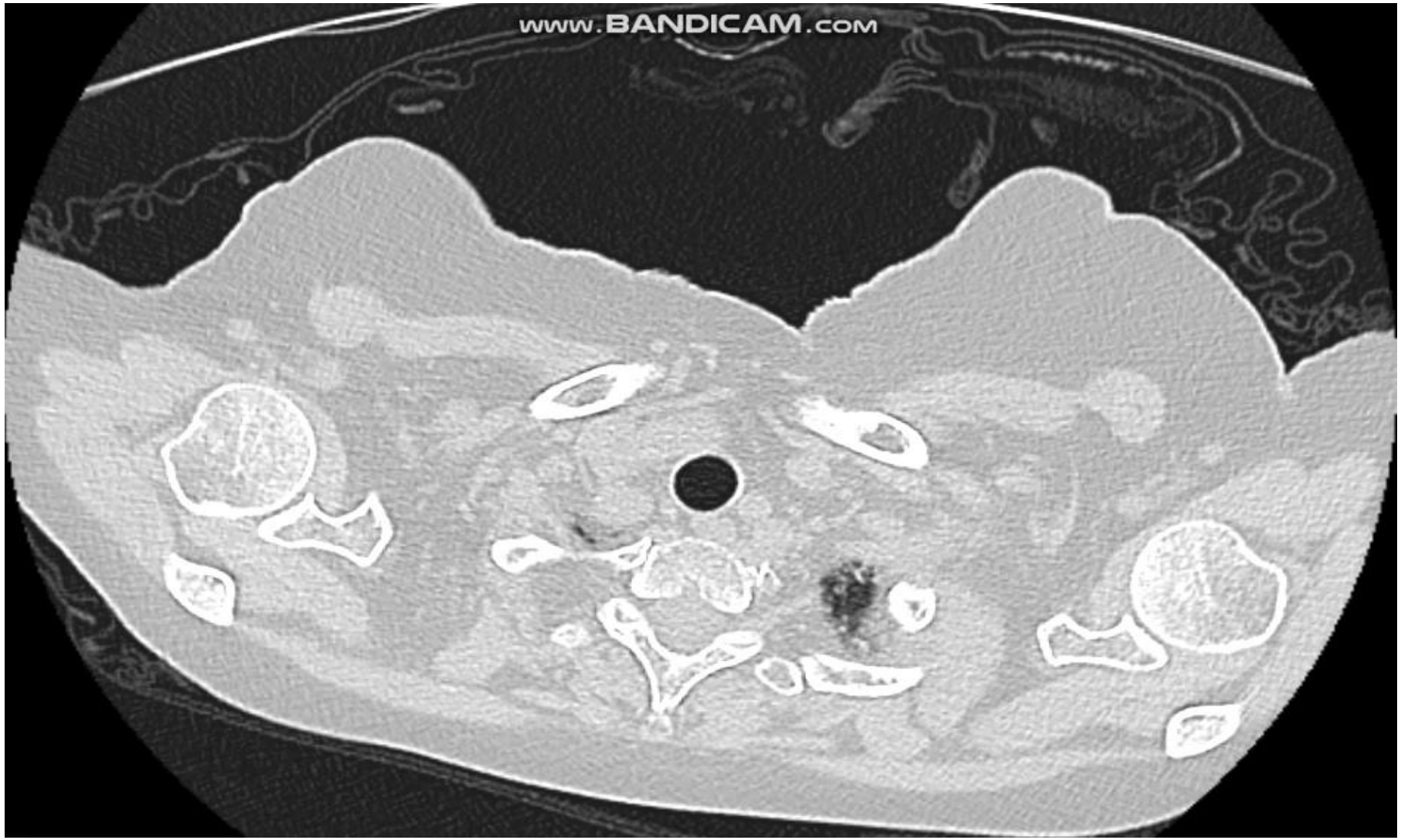
OLGU

- 54 y kadın hasta
- 4 yıldır RA hastası,
- Farklı dönemler de hidroksiklorakin, prednol, azatioprin, leflunomid kullanmış.
- En son leflunomid+ prednol alıyor.
- 4-5 aydır nefes darlığında artış tarif ediyor.

15.10.2020



23.10.2023



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GOGUS HASTALIKLARI BOLUMU
KAYSERI

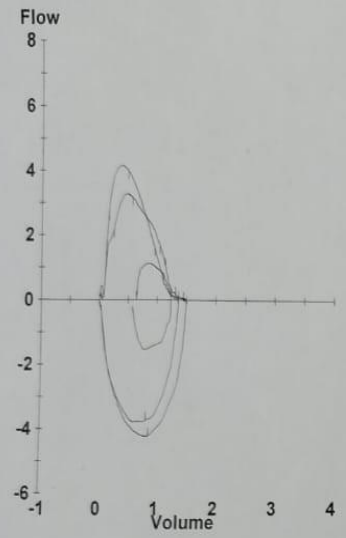
Date: 01/12/2022

[redacted]

Plethysmography Report

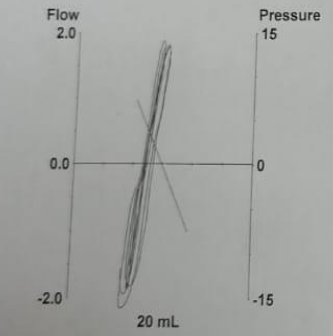
Age: 54 Height(cm): 150 Weight(kg): 58.0 Gender: Female Race: Caucasian

Technician: SAADET KOC ENGIN Temp: 25 PBar: 675



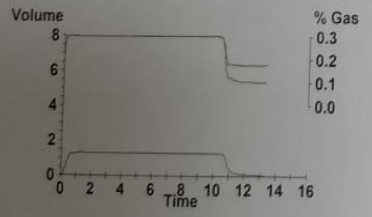
Spirometry

		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
FVC	Liters	2.35	1.37	58	1.49	64	9
FEV1	Liters	1.97	1.25	63	1.32	67	6
FEV1/FVC	%	79	91		88		
FEF25-75%	L/sec	2.96	2.74	92	2.44	82	-11
PEF	L/sec	5.52	4.14	75	4.81	87	16
FET100%	Sec		6.36		6.40		1
FIVC	Liters	2.35	1.36	58	1.48	63	9
FIF50%	L/sec		3.75		4.22		13
FVL ECode			000000		001000		
MVV	L/min						



Lung Volumes

		Ref	Pre Meas	Pre % Ref
TLC	Liters	4.11	3.41	83
VC	Liters	2.31	2.06	89
RV	Liters	1.58	1.35	85
FRC PL	Liters	2.41	1.42	59
ERV	Liters		0.07	
IC	Liters		1.99	
RV/TLC	%	37	40	
Raw	cmH2O/L/sec		2.11	
Vtg	Liters		2.28	
sGaw	L/s/cmH2O/L		0.208	



Diffusion

Hb: 11.7

		Ref	Pre Meas	Pre % Ref
DLCO	mL/mmHg/min	20.6	7.0	34
DL Adj	mL/mmHg/min	20.6	7.4	36
VA	Liters	4.11	2.02	49
DLCO/VA	mL/mHg/min/L	5.01	3.46	69
DL/VA Adj	mL/mHg/min/L	5.01	3.66	73
IVC	Liters		1.26	

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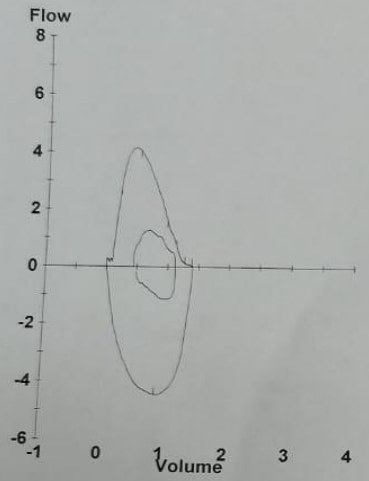
Date: 10/10/2023
Id: 66070239092
[redacted]
Height(cm): 150

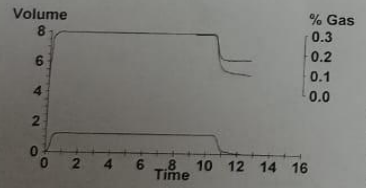
Age: 55 Race: Caucasian Gender: Female

Temp: 25 PBar: 674



Spirometry

		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
FVC	Liters	2.32	1.41	61			
FEV1	Liters	1.95	1.28	66			
FEV1/FVC	%	79	91				
FEF25-75%	L/sec	2.92	2.75	94			
PEF	L/sec	5.49	4.17	76			
FET100%	Sec		6.58				
FIVC	Liters	2.32	1.39	60			
FIF50%	L/sec		4.36				
FVL ECode			001000				
MVV	L/min						



Diffusion

Hb: 13.0

		Ref	Pre Meas	Pre % Ref
DLCO	mL/mmHg/min	20.4	6.2	30
DL Adj	mL/mmHg/min	20.4	6.3	31
VA	Liters	4.11	2.06	50
DLCO/VA	mL/mHg/min/L	4.97	3.00	60
DL/VA Adj	mL/mHg/min/L	4.97	3.04	61
IVC	Liters		1.32	

PPF Kabul Edilmeli mi?

- Evet: Radyolojik progresyon + dispnede artış

SONUÇ

- PPF oranı İPF dışı fibrotik interstisyel akciğer hastalıklarında **%13-40** oranında görülmektedir.
- PPF, İPF ile **benzer mortalite oranına** sahip bir hastalıktır.
- En sık PPF e neden olan interstisyel akciğer hastalıkları **HSP, otoimmün interstisyel akciğer hastalıkları** ve **idiopatik NSİP.**
- PPF, **alttaki hastalığın alevlenmesi değil (buzlu cam artışı değil), fibrozisin artışıdır.**
- Progresyonun mortalite ile ilişkili parametreleri **%10 veya daha fazla FVC düşüşü (en önemlisi), %5-9 relatif FVC düşüşü, %15 veya daha fazla relatif DLCO düşüşü, CT bulgularında progresyon** ve **diğer kombinasyonlardır**.

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