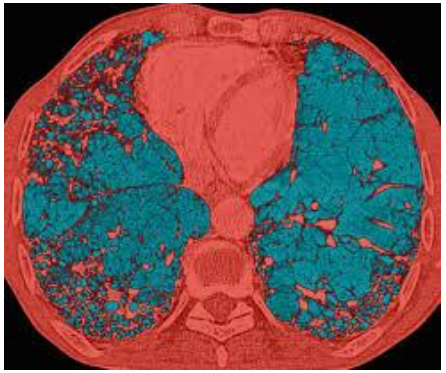
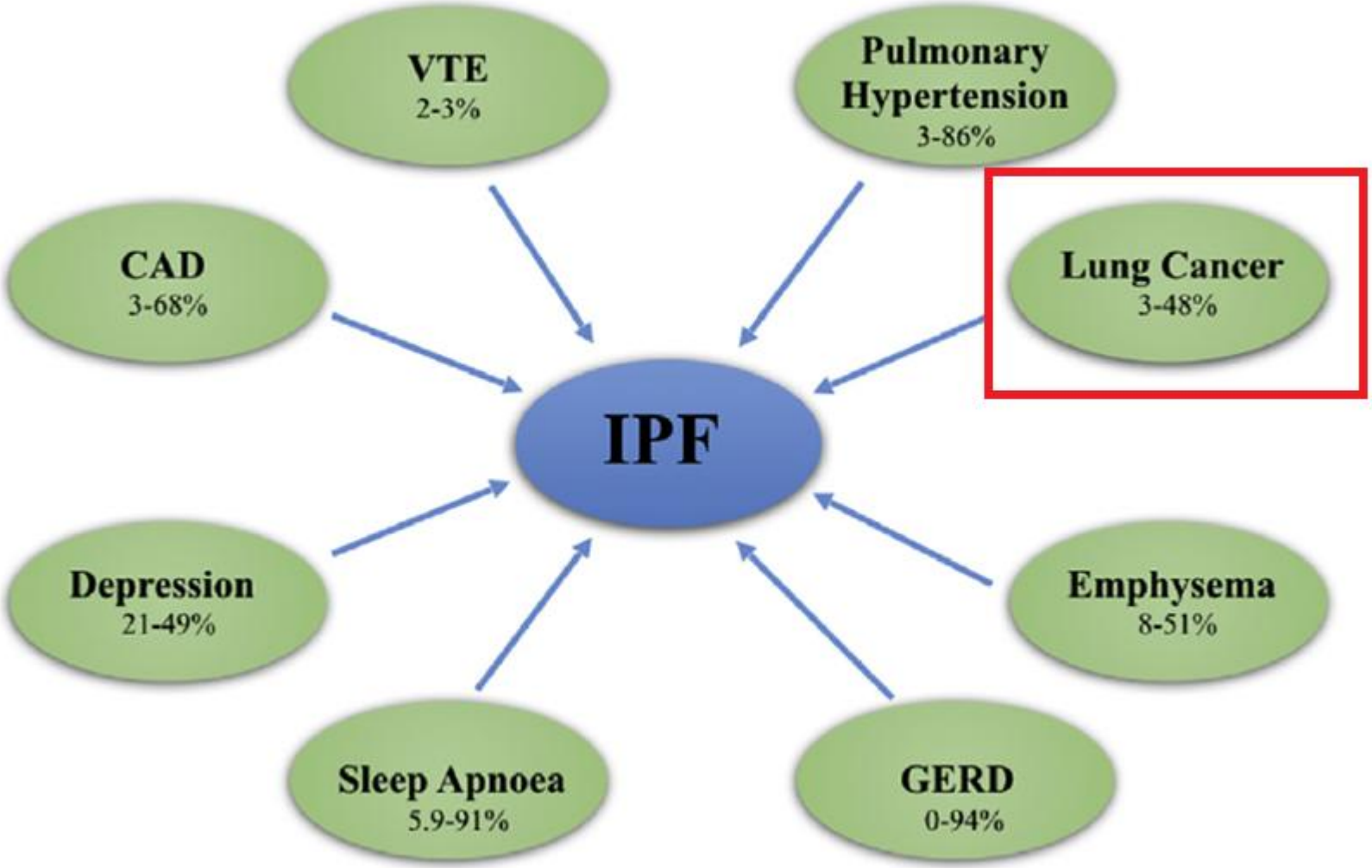
İPF ve Akciğer Kanseri



Dr Gamze KIRKIL

Fırat Üniversitesi Tıp Fakültesi

Göğüs Hastalıkları AD



Torrisi SE, et al. Pulmonary Pharmacology & Therapeutics 2018

Epidemiyoloji

*İPF hastasında akciğer kanseri gelişme riski genel popülasyona göre **5-17 kat** fazla

Le Jeune I, et al. Respir Med 2007

Jung HI, et al. Medicine 2018

*İPF hastalarında akciğer kanseri insidansı yıllar geçtikçe artar (1. yılda %1.9, 3.yılda %5.7, 5. yılda %12.3)

Suzuki T, et al. 2022

*İPF prevelansı Avrupa kohortlarında **%11.6,** Asya kohortlarında **%15.3**

Drakopanagiotakis F, et al. Cancers 2024

*Kanser hastalarının %3.7-8'inde İPF saptanıyor

Watanabe A, et al. Gen Thorac Cardiovasc Surg 2013

İPF-Kanser ortak patojenik yolaklara sahip

Proinflamatuar süreç

↓

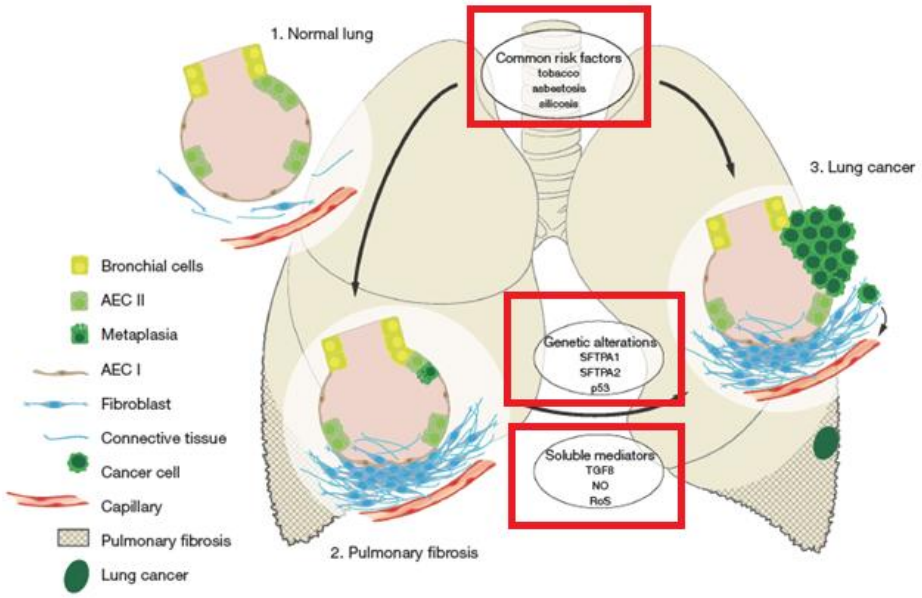
İnflamatuar hücrelerden salınan sitokinler epitel hücre proliferasyonuna neden olur

↓

Bu proliferasyon genetik değişikliklere neden olur

↓

Onkojenler aktive olur
Apoptotik genlere dönüşüm aktive olur
Tümör süpresör genler inhibe olur



Naccache JM, et al. J Thorac Dis 2018

Risk kimlerde daha fazla?

- Erkek
- Aktif smoker
- FVC'de >%10/yıl azalma
- Kombine pulmoner fibrozis amfizem varlığı

Yoo H, et al. BMC Pulm Med 2019

Tomassetti S, et al. Chest 2015

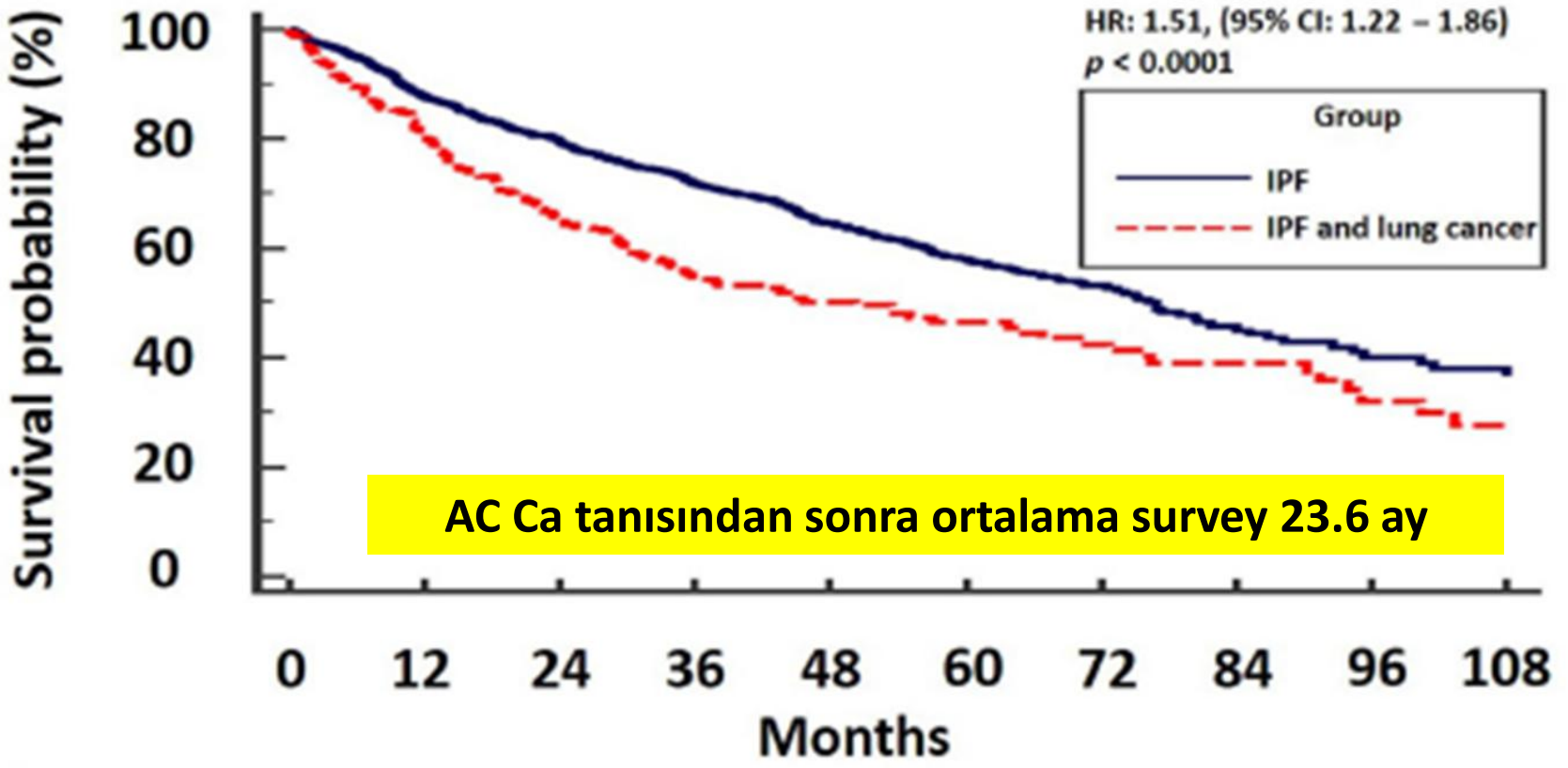
1366 İAH
Ortalama yaş 67.2 ± 12.4
639 (%46.8) erkek
227 (%16.6) hastada akciğer nodülü
55 (%24.3) hastada akciğer kanseri

Table 2
Associations of clinical risk factors with comorbid lung cancer in adults with pulmonary fibrosis.

	Univariable Analysis		
	OR	95 % CI	p-value
Age*	1.46	1.14, 1.87	0.003
Male Sex	2.60	1.17, 3.59	0.01
Weight	1.00	0.98, 1.01	0.89
BMI	0.97	0.93, 1.02	0.27
Smoking Status†			
Ever Smoker	8.33	2.51, 27.65	<0.001
Smoking Pack-years‡	1.25	1.14, 1.36	<0.001
Comorbidities			
Hypertension	1.71	0.97, 2.99	0.06
Diabetes	0.99	0.53, 1.84	0.97
Immunosuppression	0.26	0.06, 1.10	0.07
Fibrosis Pattern§			
UIP	4.31	2.11, 8.81	<0.001
CPFE	4.39	2.35, 8.21	0.009
NSIP	1.26	0.45, 3.51	0.66

Dobkin J, et al. Lung Cancer 2025

İPF hastasında Akciğer kanseri varlığı surveyi belirgin kısaltır!!!



AC Ca tanısından sonra ortalama survey 23.6 ay

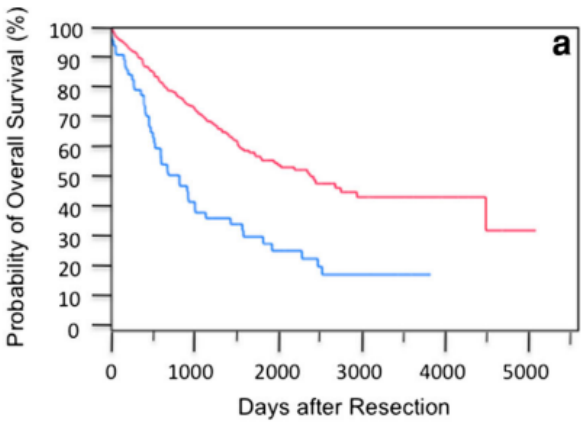
Karampitsakos T, et al. Respir 2023

İPF varlığı da kanser mortalitesini artırıyor!

Cerrahi uygulanan 387 Primer AC Ca hastası
65 (%16.8)'inde histopatolojik İPF tanısı

Table 3 Postoperative respiratory complications and short-term mortality

	Acute exacerbation	30-Day mortality	60-Day mortality	90-Day mortality
IPF (−)	0 (0 %)	3 (0.9 %)	8 (2.5 %)	17 (5.3 %)
IPF (+)	4 (6.2 %)	3 (4.6 %)	5 (7.7 %)	8 (12.3 %)
p value	<0.05	<0.05	<0.05	<0.05



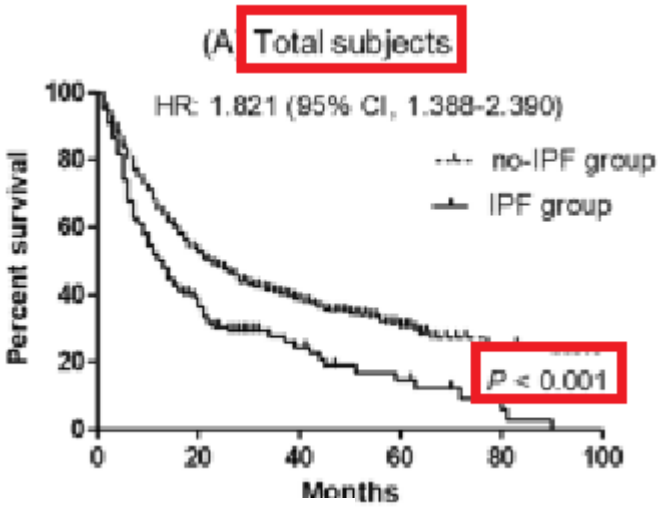
Goto T, et al. Int J Clin Oncol 2014

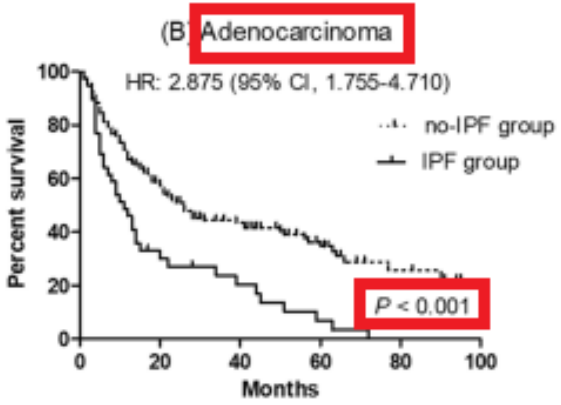
Impact of idiopathic pulmonary fibrosis on clinical outcomes of lung cancer patients

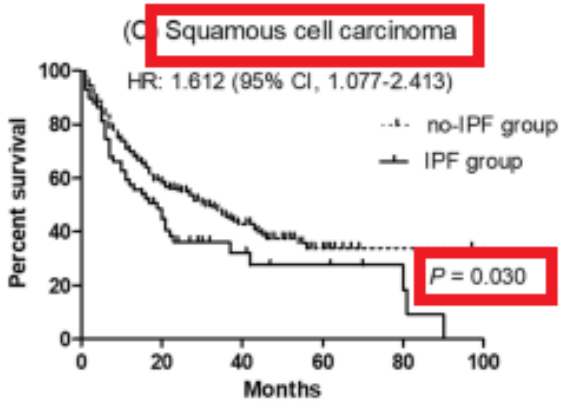
Scientific Reports | (2021) 11:8312

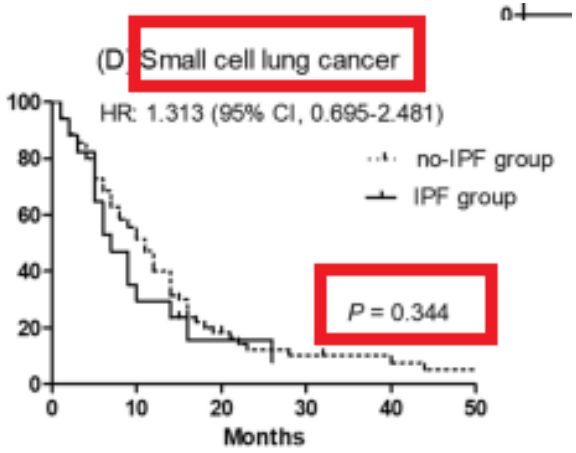
Ho Cheol Kim[1,3], Seonjeong Lee[2,3] & Jin Woo Song[1]✉

122 İPF+AC Ca,
488 AC Ca hastası
5 yıllık survey İPF grubunda %14.5,
İPF olmayan grupta %30.1









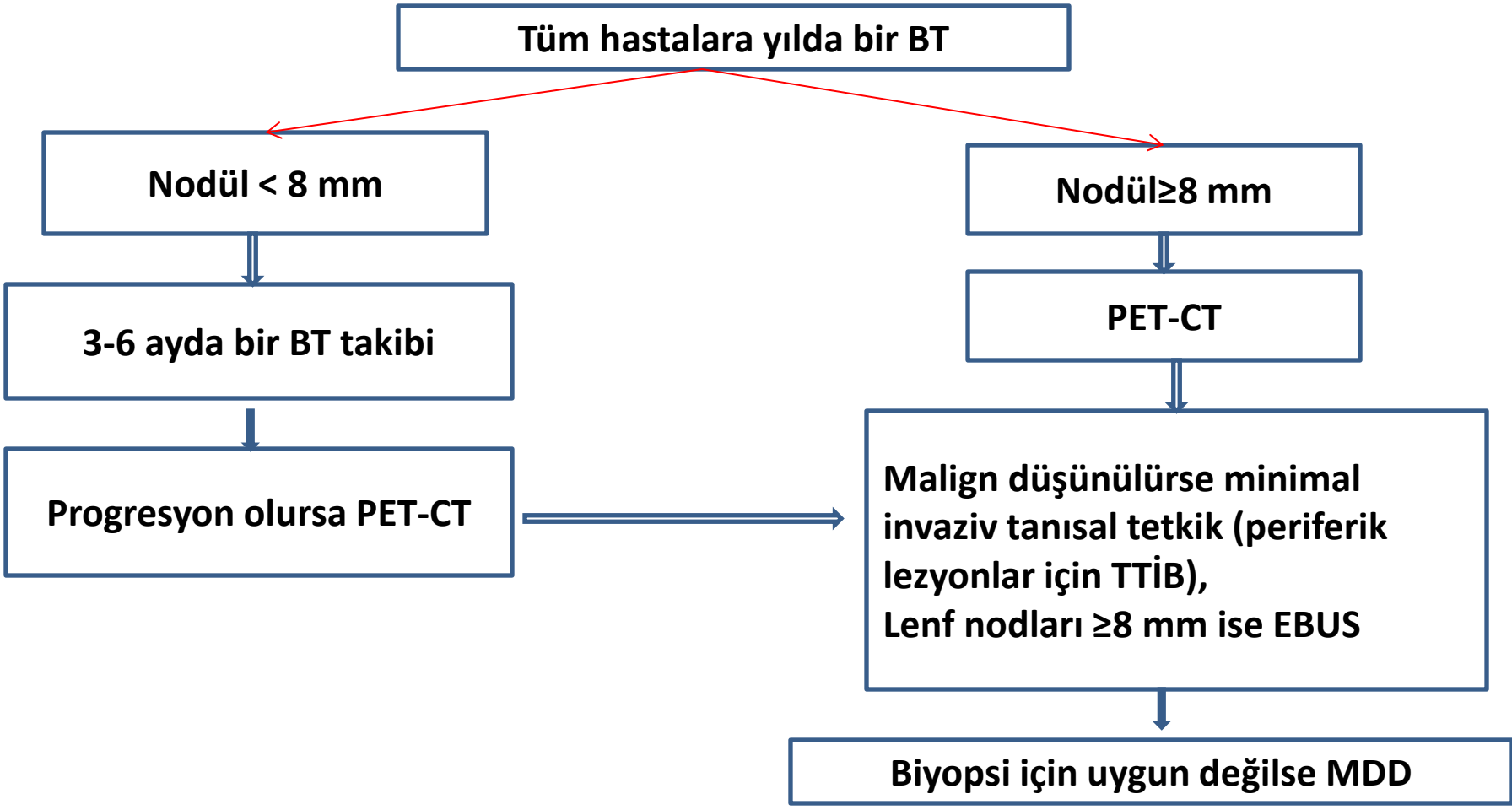
Kim HC, et al. Scientific Reports 2021

Tanısal Yaklaşım

Non-invasive and invasive strategies for diagnosing and staging lung cancer in the setting of interstitial lung disease.

Non-invasive	**CT** • Diagnosis is challenging due to background architectural distortion • Lung cancer in patients with IPF more often peripheral and in the lower lung zone • Nodules often occur at fibrotic zone of transition and demonstrate rapid growth • Reactive lymph node enlargement common in interstitial lung disease and may or may not represent metastases **FDG PET/CT** • Increased sensitivity for diagnosing local and distant metastases • Reactive lymph nodes often FDG avid
Invasive	**CT-guided PTNB** • Outpatient procedure performed with moderate sedation • Ideal for peripheral lesions Higher risk in IPF (particularly for pneumothorax) • Similar success rate for non-IPF and IPF patients **ENB and EBUS TBNA** • Outpatient procedure performed under general anesthesia • EBUS ideal for central lesions and mediastinal lymph nodes; ENB able to target more peripheral lesions • Lower risk in IPF relative to PTNB • Limited data comparing success in patients without and with ILD

Fisher DA, et al. Radiol Clin North Am. 2022



Tzouvelekis A, et al. Lancet Respir Med 2018

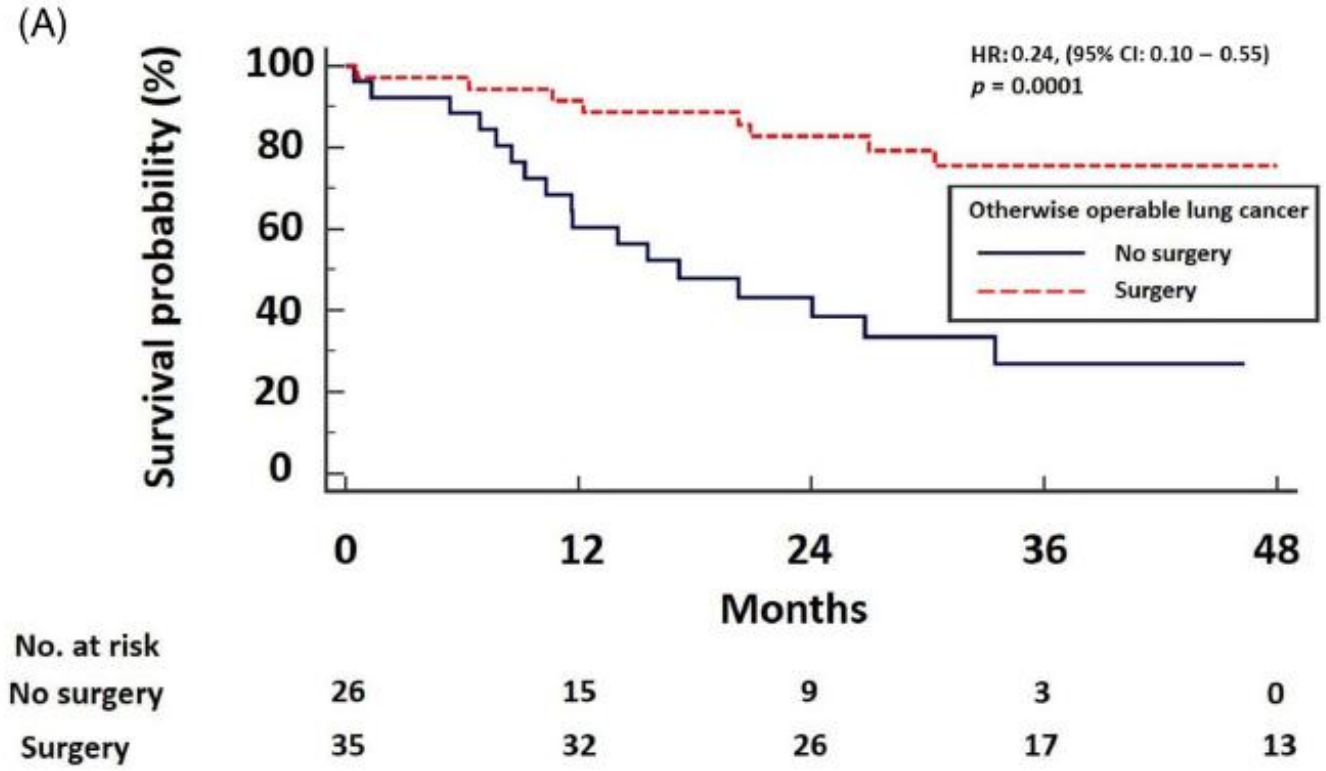
İPF + Akciğer kanseri hastasını tedavi edelim mi?

Tedavinin faydası?

Tedavinin riskleri?

Kanser tedavisinin faydası?

Cerrahi uygulanan İPF+AC kanseri hastalarında cerrahi uygulanmayanlara göre yaşam süresi **daha uzun**



Karampitsakos T, et al. Respir 2023

frontiers in Molecular Biosciences

ORIGINAL RESEARCH
published: 31 March 2021
doi: 10.3389/fmolb.2021.660800

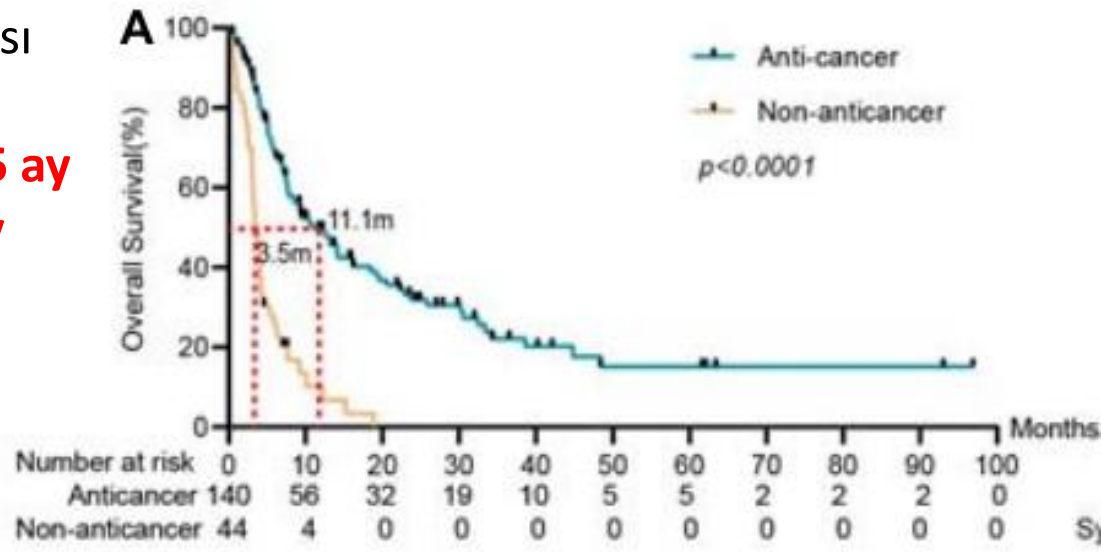
Management and Prognosis of Interstitial Lung Disease With Lung Cancer (ILD-LC): A Real-World Cohort From Three Medical Centers in China

Xie Xiaohong[1†], Wang Liqiang[1†], Li Na[2†], Lin Xinqing[1], Qin Yinyin[1], Liu Ming[1], Ouyang Ming[1], Han Qian[1], Luo Qun[1], Li Shiyue[1], Li Chunyan[3], Wang Xiaoqian[3], Yang Shuanying[2], Huang Wei[2], Liu Mei[2], Wang Ping[4] and Zhou Chengzhi[1*]*

184 İAH (%58.2'si İPF) + kanser hastası (çoğu NSCLC)

Kanser tedavisi almayanlarda OS 3.5 ay

Kanser tedavisi alanlarda OS 11.2 ay



Kanser tedavisinin riskleri?

Akut atak oranları

- Birinci basamak KT alanlarda oran %8-13

  Wang Y, et al. Front Oncol 2020
  Minegishi Y, et al. ERJ Open Res 2020

- Docetaxel verilen hastalarda oran %28, Gemcitabine verilenlerde %43

  Kenmotsu H, et al. J Thorac Oncol 2011

- ICI (nivolumab, pembrolizumab, atezolizumab) kullananlarda oran %14.5-61.5

  Nishiyama N, et al. Int J Clin Oncol 2020
  Takahara Y, et al. Thorac Cancer 2021

- Kemoradyoterapi alanlarda oran %6-83

  Saha A, et al. Clin Oncol R Coll Radiol 2022

- Cerrahi uygulananlarda %9-23

  Zanini U, et al. J Clin Med 2024

Atak riski öngörülebilir mi?

JACS risk score

Table 1 Risk scoring system for predicting acute exacerbation of interstitial pneumonia after pulmonary resection in lung cancer patients

History of acute exacerbation	5
CT findings: UIP pattern	4
Surgical procedure > wedge resection	4
Preoperative steroid use	3
Male gender	3
KL-6 > 1,000 U/mL	2
% vital capacity	1

Grade of risk	Risk score
Low risk < 10%	< 11
Intermediate risk < 10–25%	11–14
High risk < 25%	> 14

Sato T, et al. General Thoracic and Cardiovascular Surgery 2015

Postoperatif dönemde akut atak gelişiminde risk faktörleri

- Yaş>75
- BT'de; bal peteği, >%5 buzlu cam, konsolidasyon varlığı, ana pulmoner arter >28 mm
- >4 saat operasyon süresi
- Rezeke edilen dokunun genişliği
- İleri evre kanser
- Postop dönemde steroid kullanılmaması
- Karşı AC'de fibrozis skorunun yüksek olması

Naccache JM, J Thorac Dis 2018
Ozawa Y, Am J Roentgenol 2021
Iyoda A, et al. Exp Ther Med 2011
Suzuki H, et al. Surg Today 2011

Kemoterapi alanlarda akut atak gelişimini öngören skorlama

Risk skoru=

(1xantikanser ajan skoru)+(3xsigara öyküsü (>70p/yıl)+(4xsteroid öyküsü)+(3xDLCO<%50)

Skor 0-5 ise atak oranı %12, 6-10 ise %47, >11 ise %66.7

Skorlama sisteminin sensitivitesi %78.6, spesifitesi %67.8

Table 1
Anticancer Agent Score.

Risk Group	Regimen	Score
High (AE frequency ≥30%)	EGFR-TKI, amrubicin, gemcitabine, irinotecan	3
Moderate (AE frequency 11-29%)	pemetrexed, docetaxel, vinorelbin, topotecan, carboplatin/docetaxel	2
Low (AE frequency ≤10%)	carboplatin/etoposide, carboplatin/paclitaxel, cisplatin/vinorelbine, S-1	1
History of second-line chemotherapy	Any regimen	1

Isobe K, et al. Lung Cancer 2018

Kemoterapi alan hastalarda akut atak gelişiminde risk faktörleri

*Sigara öyküsü
*CRP yüksekliği
*Bazal % pred FVC düşüklüğü
*Tedavi öncesi Toraks BT'de UIP paterni varlığı
*Karşı akciğerde FDG tutulumu
*Küçük hücreli akciğer kanseri varlığı

Niwa H, et al. Mol Clin Oncol 2017
Isobe K, et al. Respirology 2010
Minegishi Y, et al. Lung Cancer 2011
Enomoto Y, et al. Lung Cancer 2016
Akaike K, Int J Clin Oncol 2020
Kenmotsu H, J Thorac Oncol 2011

Radyasyon Pnömonitis gelişiminde risk faktörleri

- FVC < %70
- Normal AC'in > %10 radyasyon uygulaması
- ECOG 2-4
- Skuamöz hücreli karsinom varlığı
- Klinik evre T2
- SBRT öncesi düzenli steroid kullanımı
- Ortalama akciğer dozu ≥ 12 Gy
- Akciğer volümünün ≥ %25'inde İAH varlığı
- Tedavi öncesi PET/CT'de tüm akciğer parankiminde SUV95>1.5 olması

Li F, et al. Radiat Oncol Lond Engl 2021
Onishi H, et al. Cancers 2018
Castillo R, Radiat Oncol Lond Engl 2014

Akut atak gelişimi önlenebilir mi?

ORIGINAL ARTICLE

Safety and effectiveness of pirfenidone combined with carboplatin-based chemotherapy in patients with idiopathic pulmonary fibrosis and non-small cell lung cancer: A retrospective cohort study

Yuji Yamamoto, Yukihiro Yano, Tomoki Kuge, Fukuko Okabe, Mikako Ishijima, Takeshi Uenami, Masaki Kanazu, Yuki Akazawa, Toshihiko Yamaguchi & Masahide Mori

Department of Thoracic Oncology, National Hospital Organization Osaka Toneyama Medical Center, Toyonaka, Japan

Thoracic Cancer **11** (2020) 3317–3325

14 İPF+NSCLC hastası

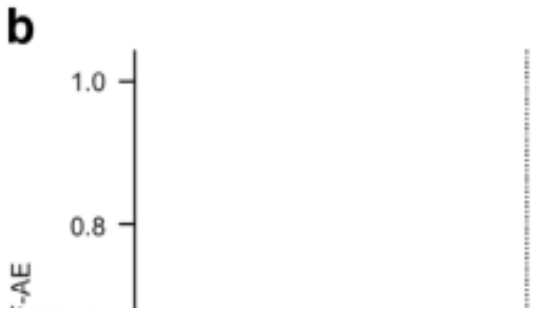
Birinci basamak kemoterapi; Pirfenidone+Carboplatin+Paclitaxel

Hastalık progrese olunca; Nivolumab, pembrolizumab

Table 4 Occurrence of acute exacerbations of idiopathic pulmonary fibrosis (AE-IPF) (n = 14)

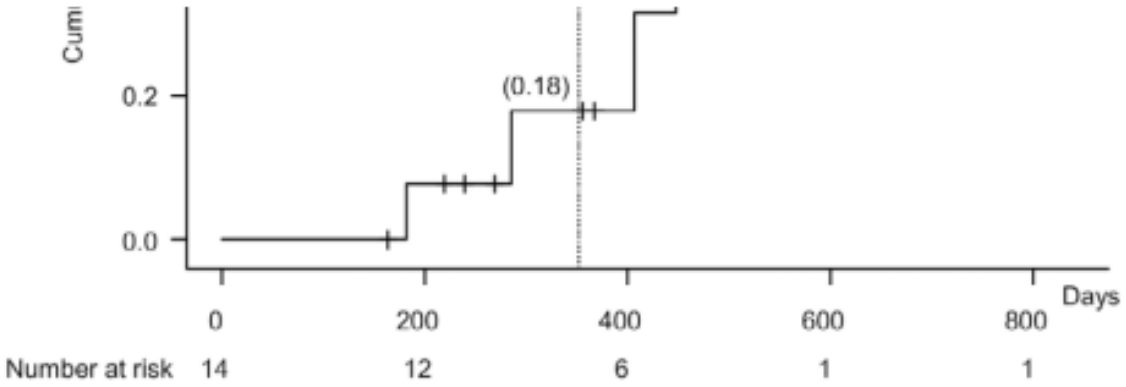
Variable	Events
Until the initiation of second-line chemotherapy, n (%)	0 (0.0)
Within 30 days from the last first-line chemotherapy administration, n (%)	0 (0.0)
Entire observation period, n (%)	4 (28.6)

Birinci basamak KT sonrası 1 yıl içinde **akut atak insidansı %18**, tüm takip döneminde **%45**



What this study adds

- Pirfenidone might have a prophylactic effect against chemotherapy-associated AE-IPF.



Nintedanib plus Chemotherapy for Small Cell Lung Cancer with Comorbid Idiopathic Pulmonary Fibrosis

Satoshi Ikeda[1], Takashi Ogura[1], Terufumi Kato[3], Hirotsugu Kenmotsu[4], Yoko Agemi[5,6], Takaaki Tokito[7], Kentaro Ito[8], Kohsuke Isomoto[9], Yuichi Takiguchi[10], Yasuto Yoneshima[11], Toshihide Yokoyama[12], Toshiyuki Harada[13], Shigeru Tanzawa[14], Nobuaki Kobayashi[15], Tae Iwasawa[2], Toshihiro Misumi[16], and Hiroaki Okamoto[5,6]

[1]Department of Respiratory Medicine and [2]Department of Radiology, Kanagawa Cardiovascular and Respiratory Center, Yokohama, Japan; [3]Department of Thoracic Oncology, Kanagawa Cancer Center, Yokohama, Japan; [4]Division of Thoracic Oncology, Shizuoka Cancer Center, Sunto-gun, Japan; [5]Department of Respiratory Medicine and [6]Department of Medical Oncology, Yokohama Municipal Citizen's Hospital, Yokohama, Japan; [7]Division of Respirology Neurology and Rheumatology, Department of Internal Medicine, Kurume University Hospital, Kurume, Japan; [8]Department of Respiratory Medicine, Matsusaka Municipal Hospital, Matsusaka, Japan; [9]Department of Medical Oncology, Kindai University Hospital, Osakasayama, Japan; [10]Department of Medical Oncology, Chiba University Hospital, Chiba, Japan; [11]Department of Respiratory Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan; [12]Department of Respiratory Medicine, Kurashiki Central Hospital, Kurashiki, Japan; [13]Department of Respiratory Medicine, Japan Community Health Care Organization Hokkaido Hospital, Sapporo, Japan; [14]Division of Medical Oncology, Department of Internal Medicine, Teikyo University School of Medicine, Itabashi-ku, Japan; [15]Department of Pulmonology, Yokohama City University Graduate School of Medicine, Yokohama, Japan; and [16]Department of Biostatistics, Yokohama City University School of Medicine, Yokohama, Japan

Ann Am Thorac Soc Vol 21, No 4, pp 635–643, Apr 2024

NEXT-SHIP çalışması; çok merkezli, faz 2 çalışma
Karboplatin+etoposid+nintedanib alan 33 hasta
Ortalama gözlem süresi 10.5 ay

Table 5. Key endpoints

Safety endpoints	*N* = 33
Incidence of IPF-AE at 28 d after last administration of cytotoxic chemotherapy, % (90% CI)	3.0 (0.2–13.6)
Median time to first IPF-AE, mo (95% CI)	Not reached
Efficacy endpoints	*N* = 32
Median survival time without IPF-AE, mo (95% CI)	12.4 (7.7–20.4)
Median progression-free survival, mo (95% CI)	4.2 (4.2–5.5)
Median overall survival, mo (95% CI)	13.4 (8.1–21.6)
Objective response	
Partial response, *n* (%)	22 (68.8)
Stable disease, *n* (%)	7 (21.9)
Progressive disease, *n* (%)	2 (6.3)
Not evaluable, *n* (%)	1 (3.1)
Objective response rate, % (95% CI)	68.8 (50.0–83.9)
Disease control rate, % (95% CI)	90.6 (75.0–98.0)

Perioperatif antifibrotik kullanımı İPF akut atak oranını azaltır

Surgery Today (2022) 52:736–744
https://doi.org/10.1007/s00595-021-02343-0

REVIEW ARTICLE

Surgical treatment for patients with idiopathic pulmonary fibrosis and lung cancer: postoperative acute exacerbation of idiopathic pulmonary fibrosis and outcomes

Akira Iyoda[1] · Yoko Azuma[1] · Susumu Sakamoto[2] · Sakae Homma[3] · Atsushi Sano[1]

Table 1 Reports on postoperative acute exacerbation of IPF in non-small-cell lung cancer patients with IPF

Author	Published year	Case number	Stage	Perioperative pirfenidone treatment	Rate of acute postoperative exacerbations	Mortality rate
Watanabe A	2008 [33]	56	p- I–IV	–	4 cases (7.1%)	4 cases (7.1%)
Saito Y	2011 [34]	28	p-IA	–	3 cases (10.7%)	1 case (3.6%)
Suzuki H	2011 [35]	28	p-I–IV	–	9 cases (32.1%)	0
Mizuno Y	2012 [36]	52	p-IA-IIIB	–	7 cases (13.5%)	6 cases (11.5%)
Sato S[a]	2018 [32]	13	p-IA, IB	–	3 cases (23.1%)	3 cases (23.1%)
Iwata T	2015 [37]	12	p-I, II or more	Pirfenidone (retro)	0	0
Iwata T	2016 [38]	31	p-IA-IV	Pirfenidone (retro)	1 case (3.2%)	–
Iwata T	2016 [39]	32	p-IA-IV	Pirfenidone (phase II)	1 case (3.1%)	1 case (3.1%)
Sekihara K	2020 [40]	36	p-I–III	Pirfenidone (retro)	3 cases (8.3%)	1 case (2.8%)
Kanayama M	2020 [41]	28	p-IA-IIIA	Pirfenidone (retro)	1 case (3.6%)	–

İPF + Akciğer Kanseri Tedavisi

Comparison of available lung cancer treatments in the setting of interstitial lung disease.

Treatment	Definitive therapy?	Benefits	Risk of acute exacerbation	Unique risks
Surgery	Yes	Gold standard	0-20%, increases with extent of resection and perioperative factors	Most invasive; permanent reduction in vital capacity
Stereotactic body radiotherapy	Yes	Non-invasive	18-20.5%	Radiation pneumonitis; can reduce lung function
Percutaneous thermal ablation	Yes	Minimally invasive, no permanent decrease in lung function (in absence of acute exacerbation)	18%	Shares some risks with surgery (e.g., pneumothorax, bronchopleural fistula, prolonged air leak)
Systemic therapy	No	Non-invasive	13-50%	Immunosuppression from certain agents/ regimens

Fisher DA, et al. Radiol Clin North Am. 2022

Stage of NSCLC	Treatment Options for NSCLC with ILD
Stage I	- Surgical resection (lobectomy or segmentectomy): for patients with stable and well-controlled ILD, with mild to moderately impaired lung function - Stereotactic body radiation therapy (SBRT): alternative to surgery for patients who are not surgical candidates due to their ILD, due to poor lung function or comorbidities. Option in a minority of very carefully selected patients due to the possible detrimental risk of pneumonitis - Percutaneous image-guided ablation to be considered in patients with poor lung function and small tumors
Stage II	- Surgical resection: for patients with stable and well-controlled ILD, with mild to medium impaired lung function - SBRT: For patients unsuitable for surgery due to ILD, SBRT may be considered. Option in a minority of very carefully selected patients due to the possible detrimental risk of pneumonitis
Stage III	- Radio chemotherapy: standard of treatment for locally advanced NSCLC. Decision to proceed in patients with ILD to be taken in oncology board, considering the high potential risk of pulmonary toxicity. Sequential, instead of concomitant therapy may be associated with reduced risk of pulmonary toxicity. Radiation therapy may be an option in a small minority of very carefully selected patients due to the possible detrimental risk of pneumonitis - Immunotherapy: may be considered in patients with stable ILD and mild to moderately impaired lung function, as part of the treatment regimen
Stage IV	- Systemic therapy: chemotherapy, targeted therapy, immunotherapy, or a combination of the above depending on the patient's performance status, ILD status and comorbidities - Palliative care: in advanced stages of NSCLC or end-stage ILD

Drakopanagiotakis F, et al. Cancers 2024

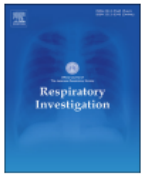
İPF+Akciğer Kanseri Tedavisi Yönetiminde Rehber/Uzlaşı Raporu Önerileri

RESPIRATORY INVESTIGATION 57 (2019) 512–533

Available online at www.sciencedirect.com

Respiratory Investigation

journal homepage: www.elsevier.com/locate/resinv



Statement

Summary of the Japanese Respiratory Society statement for the treatment of lung cancer with comorbid interstitial pneumonia

Molecular-targeted drugs and ICI are poorly suited for lung cancer patients with comorbid IP [6–7]. At present, clinicians must decide the therapeutic indications and the regimen based on their own experience. The establishment of a guideline is needed.

6.1.4.1. Selection of chemotherapy for NSCLC with comorbid IP

Table 4 – Study of combination chemotherapy including platinum preparation for NSCLC with comorbid IP

Author	Regimen	N	Study design	AE (%)	Median OS
Minegishi [5]	CBDCA + weekly PTX	18	Prospective	1 (5.6%)	10.6 m
Sekine [6]	CBDCA + S1	21	Prospective	2 (10%)	9.7 m
Shukuya [20]	CBDCA (weekly or monthly) + weekly PTX	15	Retrospective	4 (27%)	7.0 m
Kinoshita [48]	Any	22	Retrospective	3 (14%)	5.4 m
Okuda [27]	Platinum + VNR	19	Retrospective	3 (16%)	7.4 m
Watanabe [26]	CDDP + VNR	67	Retrospective	7 (10.4%)	7.4 m
Shimizu [19]	CBDCA + PTX	11	Retrospective	0 (0%)	9.7 m
Shimizu [19]	CBDCA + PTX + Bv	10	Retrospective	1 (10%)	16.1 m
Enomoto [49]	CBDCA + PTX + Bv	25	Retrospective	3 (12%)	8.5 m
Kenmotsu [18]	Any	104	Retrospective	9 (9%)	9.9 m

AE, acute exacerbation of IP; OS, overall survival; CBDCA, carboplatin; PTX, paclitaxel; VNR, vinorelbine; Bv, bevacizumab.

6.1.4.2. *Selection of chemotherapy for Small-cell lung cancer (SCLC) with comorbid IP*

- The options for first-line chemotherapy in SCLC are limited compared to NSCLC, but a consensus has been reached to make the standard treatment, a platinum preparation with concomitant etoposide therapy, and the standard treatment for cases with comorbid IP [9–12].
- It is expected that second-line chemotherapy also improves prognosis of recurrent SCLC with comorbid IP [13–14]. However, the risk of AE may be greater than in first-line chemotherapy. It is hoped that future research

- Chemoradiation therapy is not recommended for limited-disease (LD)-SCLC with comorbid IP at present, because thoracic radiotherapy carries a high risk of AE of IP [16,17]. It is unknown whether radiotherapy could be possible if patients are selected appropriately.

Lung cancer in patients with fibrosing interstitial lung diseases: an overview of current knowledge and challenges

Namrata Kewalramani[1], Carlos Machahua[1,2], Venerino Poletti[3], Jacques Cadranel[4], Athol U. Wells[5] and Manuela Funke-Chambour[1,2]

TABLE 1 Suggestions for treatment of lung cancer in fibrosing interstitial lung disease (fILD)

Suggestions based on the available studies:
The choice of treatment with chemotherapy should be carefully made by analysis of the risk/benefit balance. Patient selection and careful counselling are crucial.
Carboplatin plus weekly (nab-)paclitaxel for four (or six) cycles remains the first-line standard therapy in fit NSCLC fILD patients without maintenance therapy.
Addition of bevacizumab should be considered in fit nonsquamous NSCLC patients.
Vinorelbine (squamous) and pemetrexed (adenocarcinoma) monotherapy should be administered in a second-line setting.
Carboplatin etoposide for four cycles (or six cycles) remain the standards of care for SCLC.
Drugs that are not recommended: gemcitabine and docetaxel.

Kewalramani N, et al. ERJ Open Res 2022

fİAH + NSCLC Hastalarında Tedavi

Treatment	Stage I–IB	Stage IIA–IIIA	Stage IIIB/C	Stage IV		
Standard	Lobectomy VATS No adjuvant chemotherapy		Treat as stage IV?	Carboplatin weekly (nab-)paclitaxel (± bevacizumab)	Carboplatin weekly (nab-)paclitaxel (± bevacizumab) Nivolumab/pembrolizumab second line?	Carboplatin weekly (nab-)paclitaxel (± bevacizumab)
Option/not fit	SBRT Sublobar resection	Treat as stage IV?	Treat as stage IV?	Kinase inhibitors?	Mono-chemotherapy Paclitaxel, vinorelbine, pemetrexed	
Frail/oldest patients/PS2	SBRT	Palliative care	Palliative care	Kinase inhibitor	Palliative care	Palliative care

Kewalramani N, et al. ERJ Open Res 2022

Antifibrotiklerin kemoterapötik etkinliği var mı?

NSCLC hastalarında nintedanib kullanımı

Table 2 Nintedanib phase II to phase III clinical trials

Phase	Reference	Patient characteristics	*n*	Treatment	ORR (%)	Median PFS	Median OS
III	Reck *et al.*[8]	NSCLC second-line	1314	Docetaxel + Nintedanib 200 mg/b.i.d. vs. Docetaxel	NE	3.4 vs. 2.7 months	10.1 vs. 9.1 months
II	Reck *et al.*[11]	NSCLC second- or third-line	73	Nintedanib 250 mg/b.i.d. or 150 mg/b.i.d.	NE	6.9 weeks	21.9 weeks
III	Hanna *et al.*[12]	Nonsquamous NSCLC previously treated	713	Pemetrexed + Nintedanib 200 mg/b.i.d. vs. Pemetrexed	9.1 vs. 8.3	4.4 vs. 3.6 months	12.0 vs. 12.7 months

NE, not evaluated; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; Sq, squamous.

Shiratori T, et al. Thoracic Cancer 2020

Thoracic Cancer
Open Access
Thoracic Cancer ISSN 1759-7706
Thoracic Cancer **11** (2020) 1720–1723

CASE REPORT

Effect of nintedanib on non-small cell lung cancer in a patient with idiopathic pulmonary fibrosis: A case report and literature review

Toshihiro Shiratori[1], Hisashi Tanaka[1], Chiori Tabe[1], Junichiro Tsuchiya[1], Yoshiko Ishioka[1], Masamichi Itoga[1], Kageaki Taima[1], Shingo Takanashi[2] & Sadatomo Tasaka[1]

1 Department of Respiratory Medicine, Hirosaki Uni

69 y, ileri evre NSCLC
3 kür KT sonrası progresyon
KT stoplanıp nintedanib başlanıyor
1 ay sonra parsiyel remisyon

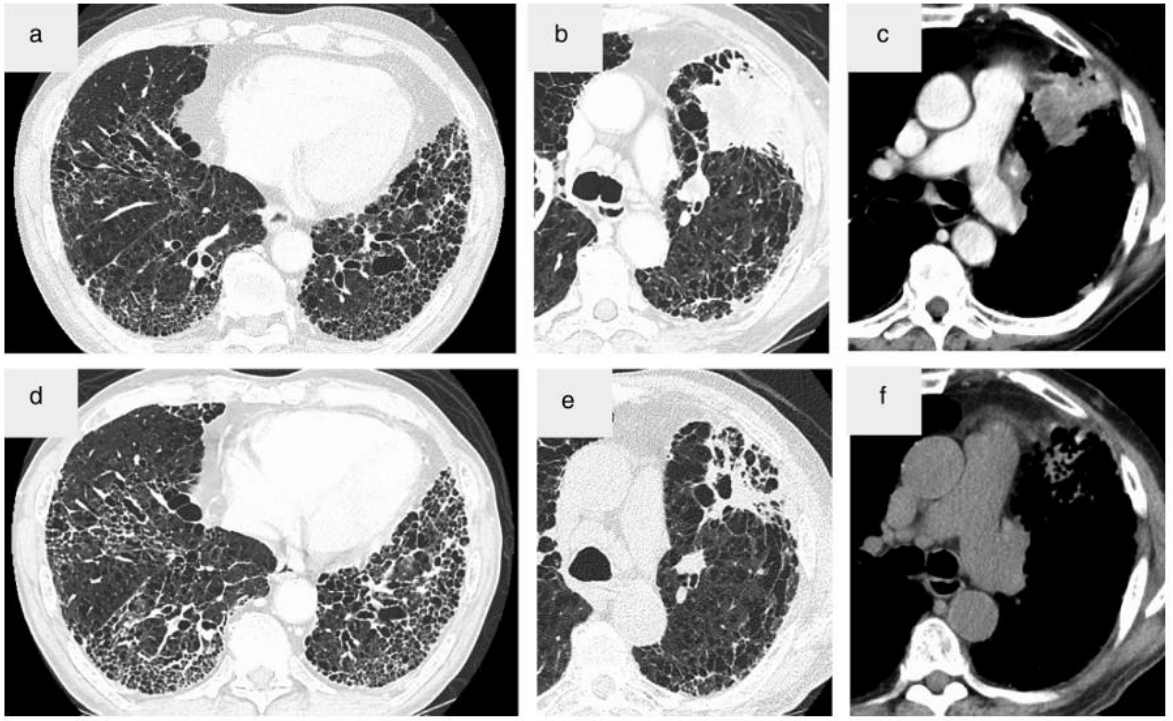


Figure 2 (**a**) Chest computed tomography (CT) scan at initial referral to our hospital showed honeycomb lung, traction bronchiectasis in the dorsal side of both lung bases and interstitial lung disease of usual interstitial pneumonia pattern. (**b**) CT scan on the initiation of nintedanib showed a solid mass measuring 50 mm in diameter in the left upper lobe, (**c**) with pleural dissemination and (**d**) that the interstitial pneumonia was getting worse. (**e**) CT scan taken one month after the initiation of nintedanib showed regression of the primary lesion and (**f**) pleural disseminated lesions in the left

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DOI: 10.1111/1759-7714.13935

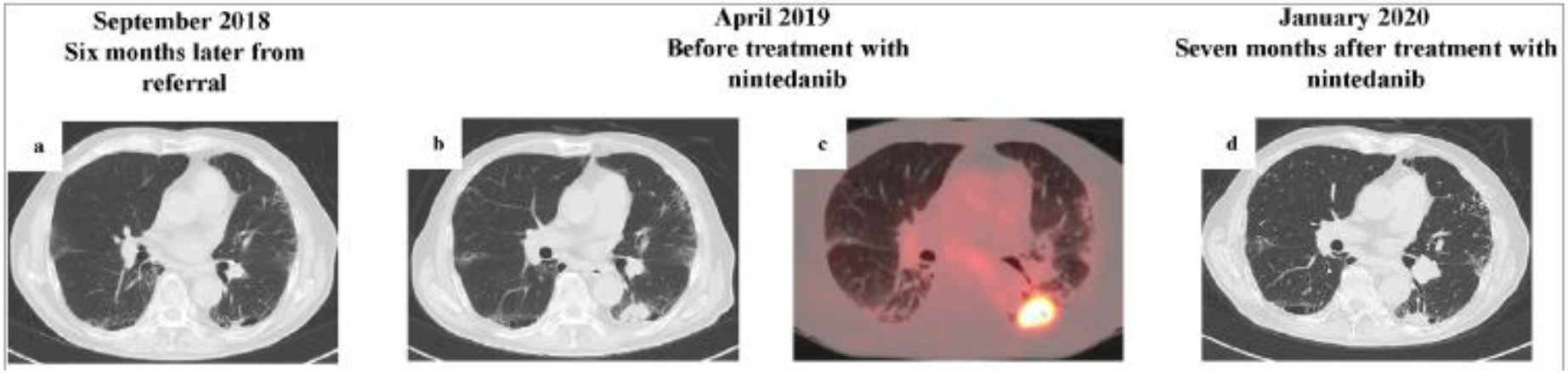
CASE REPORT

WILEY

Remarkable response of non-small cell lung cancer to nintedanib treatment in a patient with idiopathic pulmonary fibrosis

Yoshiro Kai[1] | Masayuki Matsuda[1] | Atsuhiko Fukuoka[2] | Shigeto Hontsu[3] | Motoo Yamauchi[3] | Masanori Yoshikawa[3] | Shigeo Muro[3]

82 yaş İPF+ NSCLC (Skuamöz)
Sadece destek tedavi ve İPF için nintedanib başlanıyor
7 ay sonra BT'de parsiyel yanıt izleniyor



Mediavilla-Varela *et al. BMC Cancer* (2016) 16:176
DOI 10.1186/s12885-016-2162-z

BMC Cancer

RESEARCH ARTICLE Open Access

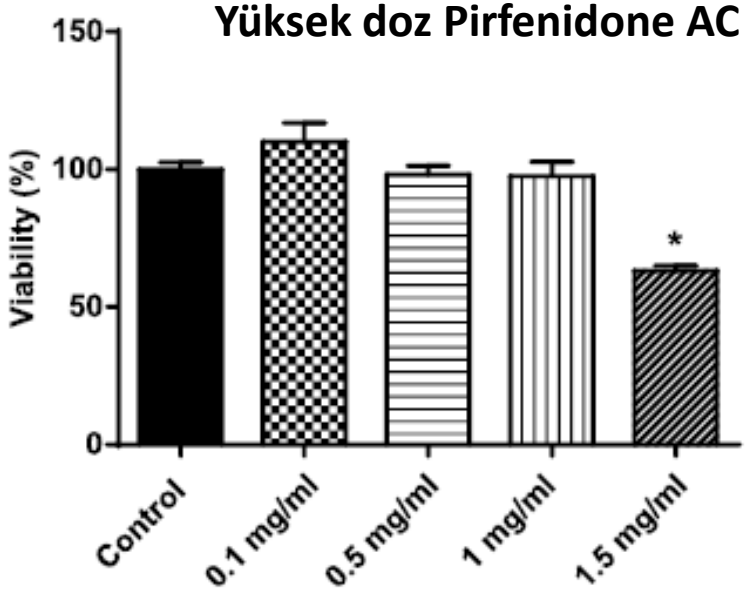
The anti-fibrotic agent pirfenidone synergizes with cisplatin in killing tumor cells and cancer-associated fibroblasts

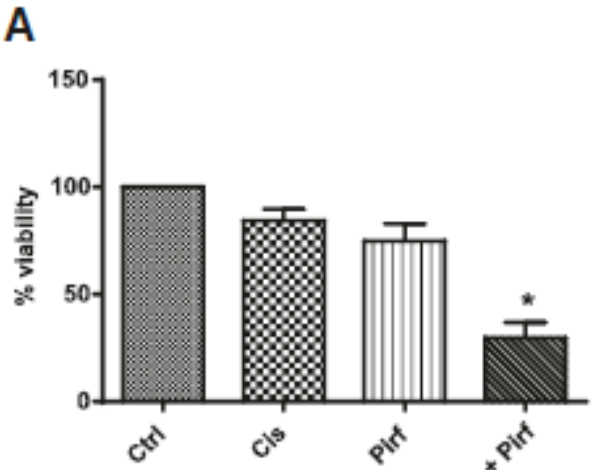
Melanie Mediavilla-Varela[1], Kingsley Boateng[1], David Noyes[1] and Scott J. Antonia[1,2*]

A549 hücreleri ve kanser ilişkili fibroblastlar (CAF), 6 hflık farelere sc olarak enjekte ediliyor
Tümör palpe edilecek boyuta ulaştığında fareler 4 gruba ayrılıyor:
Grup 1: günlük ip kontrol vehicle (H20)
Grup 2: 27 gün boyunca pirfenidone 200 mg/kg
Grup 3: cisplatin 5 mg/kg 0,3,6,21,24,27. günlerde
Grup 4: pirfenidone+cisplatin

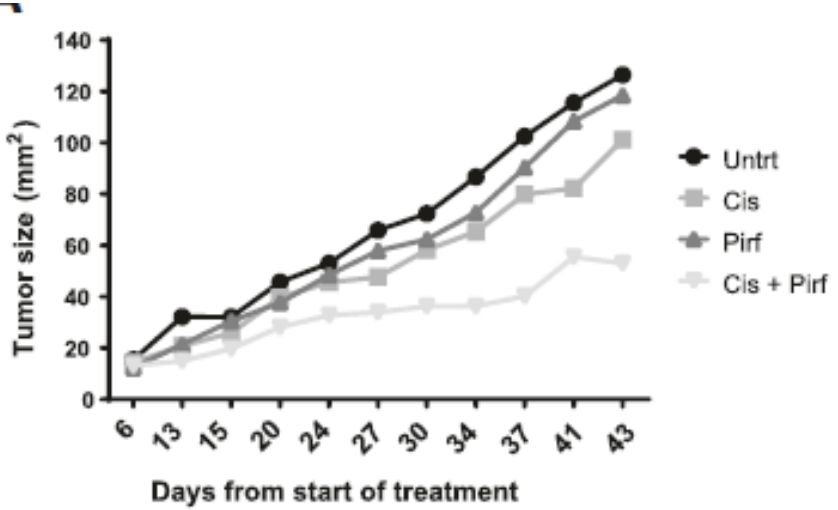
A

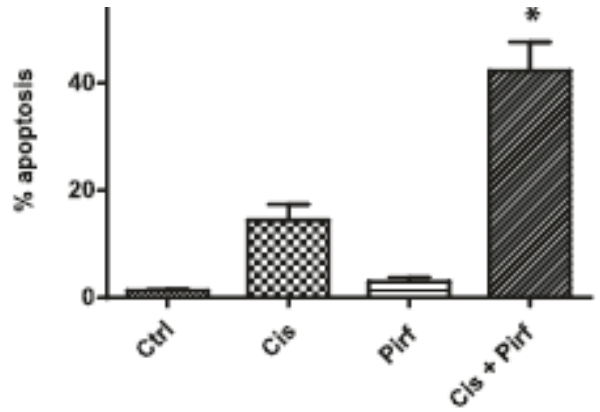
Yüksek doz Pirfenidone AC CAF proliferasyonunu %40 azaltıyor





Conclusions: Our studies reveal for the first time that the combination of cisplatin and pirfenidone is active in preclinical models of NSCLC and therefore may be a new therapeutic approach in this disease.





A: PFD+Cis tedavisinden 72 saat sonra A459 hc canlılığı azalıyor B. Apopitozis artıyor

Lung Cancer 106 (2017) 8–16

Contents lists available at ScienceDirect

Lung Cancer

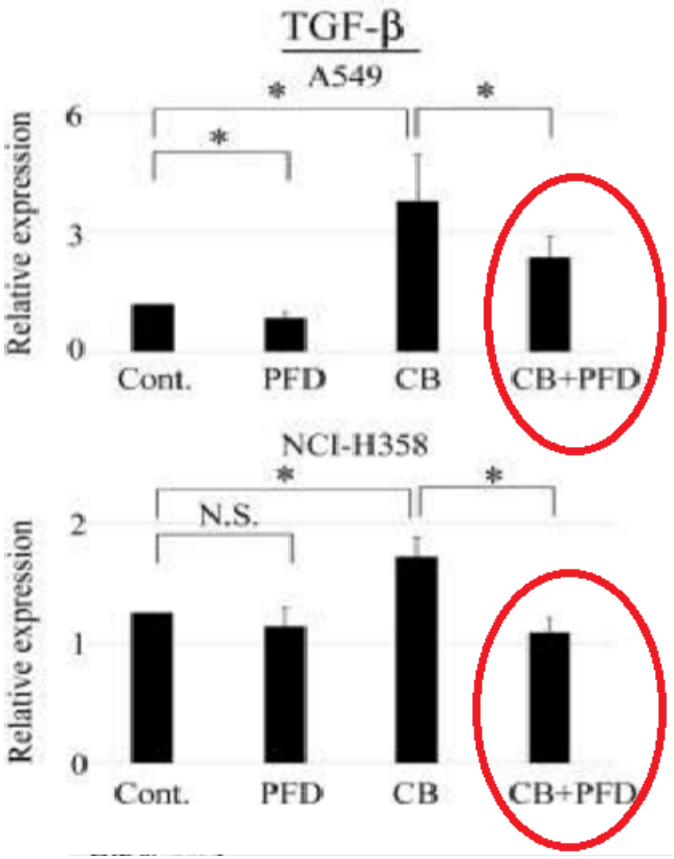
journal homepage: www.elsevier.com/locate/lungcan

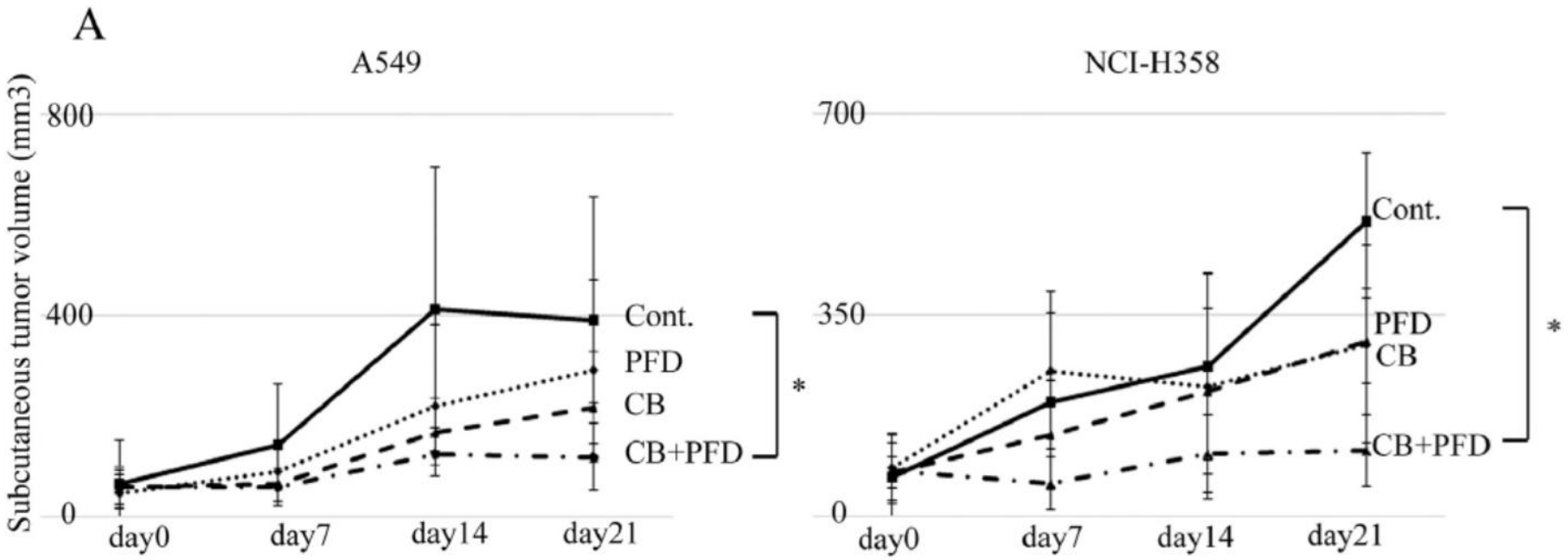
Pirfenidone plays a biphasic role in inhibition of epithelial-mesenchymal transition in non-small cell lung cancer

Ayako Fujiwara, Yasushi Shintani*, Soichiro Funaki, Tomohiro Kawai
Masato Minami, Meinoshin Okumura

Department of General Thoracic Surgery, Osaka University Graduate School of Medicine, Osaka, Japan

A549 ve NCI-H358 hücreleri 4 haftalık dişi farelerin sırtına sc enjekte ediliyor
3 hafta sonra fareler 4 gruba ayrılıyor:
Kontrol grubu
Pirfenidone grubu (ip 200 mg/kg karboplatinden sonra her gün-42. güne kadar)
Karboplatin grubu (21. günde 120 mg/kg ip)
PFD+karboplatin grubu





Conclusions: PFD could attenuate the EMT process induced not only by exogenous TGF-β1 but also by paracrine TGF-β produced from NSCLC cells. PFD may be a promising new therapeutic agent for the treatment of NSCLC through the regulation of EMT.

Kanser gelişimini engelleyebilir miyiz?

RESPIRATORY INVESTIGATION 56 (2018) 72–79

Contents lists available at ScienceDirect

Respiratory Investigation

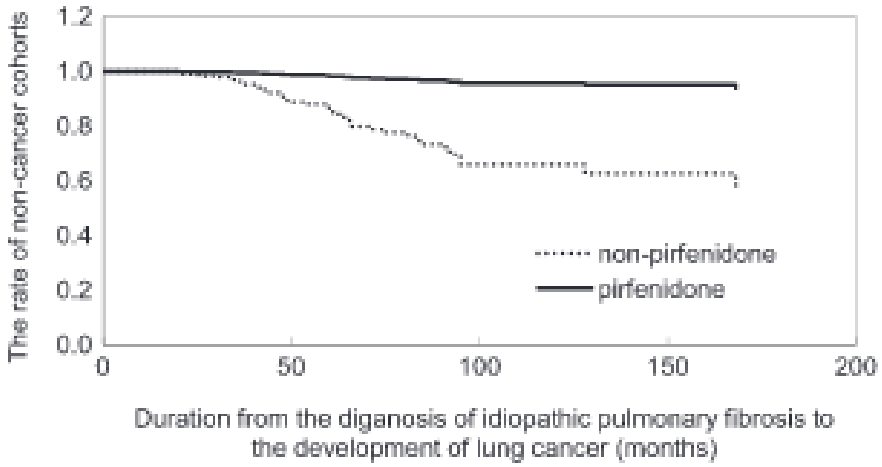
journal homepage: www.elsevier.com/locate/resinv

Original article

Reduced incidence of lung cancer in patients with idiopathic pulmonary fibrosis treated with pirfenidone

Yukiko Miura[a,b,*], Takefumi Saito[a], Toru Tanaka[a], Hiroyuki Takoi[a], Yohei Yatagai[a], Minoru Inomata[b], Takahito Nei[c], Yoshinobu Saito[b], Akihiko Gemma[b], Arata Azuma[b]

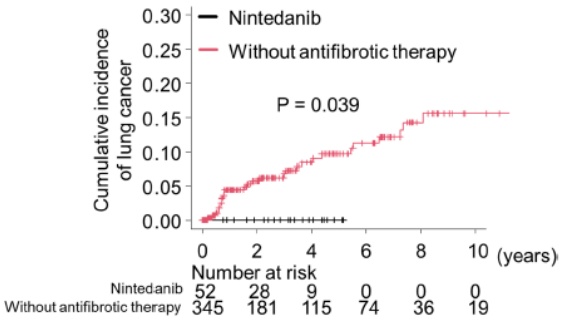
PFD grubunda kanser insidansı %2.4 (2/83), non-PFD grubunda %22.0 (39/178), p<0.0001



Impact of antifibrotic therapy on lung cancer development in idiopathic pulmonary fibrosis

Hyogo Naoi,[1] Yuzo Suzuki ,[1] Kazutaka Mori,[2] Yuya Aono,[1] Masato Kono,[3] Hirotsugu Hasegawa,[4] Koshi Yokomura,[4] Yusuke Inoue,[1] Hironao Hozumi ,[1] Masato Karayama,[1] Kazuki Furuhashi,[1] Noriyuki Enomoto,[1] Tomoyuki Fujisawa , Yutaro Nakamura,[1] Naoki Inui,[1] Hidenori Nakamura,[3] Takafumi Suda[1]

Thorax 2022;**77**:727–730. doi:10.1136/thoraxjnl-2021-218281



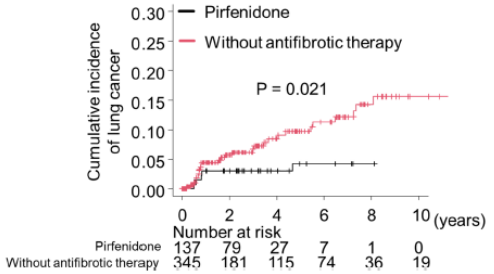


Table 2 Incidence and prevalence of LC and rate of LC-related mortality in patients with IPF treated with or without antifibrotic therapy

	All patients (N=345)	IPF-antifibrotic therapy (+) patients (n=189)	IPF-antifibrotic therapy (–) patients (n=156)	Risk ratio*
LC cases, n	35	5	30	
Incidence, per 100 person-years (95% CI)	2.14 (1.50 to 2.96)	1.07 (0.35 to 2.47)	4.53 (3.08 to 6.41)	0.235 (0.092 to 0.602)
Prevalence, % (95% CI)	10.1 (7.2 to 13.8)	2.65 (0.86 to 6.07)	19.2 (13.4 to 26.3)	0.138 (0.055 to 0.346)
LC-related mortality, % (95% CI)	7.9 (4.7 to 12.1)	1.61 (0.20 to 5.70)	15.2 (9.0 to 23.6)	0.106 (0.025 to 0.450)

Pirfenidone and risk of lung cancer development in idiopathic pulmonary fibrosis: a nationwide population-based study

Hee-Young Yoon[1], Hoseob Kim[2], Yoonjong Bae[2] and Jin Woo Song[3]

[1]Division of Allergy and Respiratory Diseases, Department of Internal Medicine, Soonchunhyang University Seoul Hospital, Seoul, Republic of Korea. [2]Department of Data Science, Hanmi Pharmaceutical Co., Ltd, Seoul, Republic of Korea. [3]Department of Pulmonary and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea.

Eur Respir J 2025; 65: 2401484

TABLE 2 Incidence of lung cancer in patients with idiopathic pulmonary fibrosis according to pirfenidone use and treatment duration

	Patients	Lung cancer	Incidence[#] (95% CI)
Total population	19 614	1355 (6.9)	17.8 (16.9–18.8)
Pirfenidone usage			
No	9952	925 (9.1)	27.9 (26.1–29.7)
Yes	9662	431 (4.7)	10.4 (9.5–11.4)
Duration			
<1 month	11 109	925 (8.3)	24.8 (23.2–26.4)
⩾1 month	8505	431 (5.1)	11.1 (10.1–12.2)
<6 month	13 594	1083 (8.0)	22.4 (21.1–23.8)
⩾6 months	6020	273 (4.5)	9.8 (8.7–11)
<1 year	15 303	1189 (7.8)	21.2 (20–22.5)
⩾1 year	4311	167 (3.9)	8.3 (7.1–9.6)
<2 year	17 553	1282 (7.3)	19.6 (18.6–20.7)
⩾2 years	2060	73 (3.5)	6.8 (5.4–8.5)

Data are presented as n or n (%), unless otherwise stated. [#]: cases per 1000 person-years.

Conclusion: Pirfenidone use may be associated with a reduced lung cancer risk in patients with IPF.

TABLE 4 Age- and sex-stratified subgroup analysis for association between pirfenidone and risk of lung cancer in patients with idiopathic pulmonary fibrosis

	Weighted HR		Weighted adjusted HR#	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age¶		0.941+		0.549+
<65 years	0.351 (0.288–0.429)	<0.001	0.336 (0.274–0.412)	<0.001
⩾65 years	0.356 (0.310–0.409)	<0.001	0.356 (0.310–0.410)	<0.001
Sex¶		0.119+		0.096+
Male	0.338 (0.300–0.380)	<0.001	0.337 (0.299–0.379)	<0.001
Female	0.503 (0.318–0.796)	0.003	0.519 (0.327–0.823)	0.005

Subgroup analyses

When stratified by age (⩾65 *versus* <65 years), pirfenidone consistently reduced lung cancer risk in both age groups (<65 years: weighted adjusted HR 0.336, 95% CI 0.274–0.412; ⩾65 years: weighted adjusted HR 0.356, 95% CI 0.310–0.410) (table 4). When stratified by sex, the reduction in risk was also consistently significant in males (weighted adjusted HR 0.337, 95% CI 0.299–0.379) and females (weighted adjusted HR 0.519, 95% CI 0.327–0.823) (table 4).

RESEARCH ARTICLE

The preventative effects of statin on lung cancer development in patients with idiopathic pulmonary fibrosis using the National Health Insurance Service Database in Korea

Yoo Jung Lee[1], Nayoon Kang[2], Junghyun Nam[3], Eung Gu Lee[4], Jiwon Ryoo[4], Soon Seog Kwon[4], Yong Hyun Kim[4], Hye Seon Kang[4]*

1 Department of Internal Medicine, Division of Pulmonary, Allergy and Critical Care Medicine, Incheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Incheon, Republic of Korea, 2 Department of Statistics and Data Science, Yonsei University, Seoul, Republic of Korea, 3 Department of Internal Medicine, Division of Respiratory, Allergy and Critical Care Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea, 4 Department of Internal Medicine, Division of Respiratory, Allergy and Critical Care Medicine, Bucheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Bucheon, Republic of Korea

PLOS ONE | https://doi.org/10.1371/journal.pone.0299484 March 13, 2024

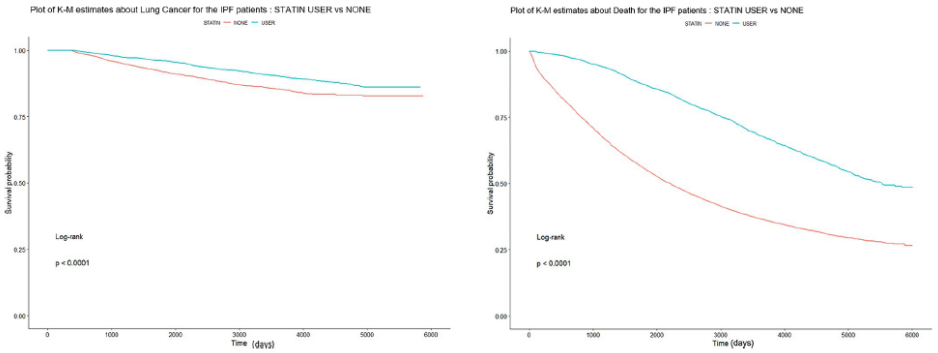


Fig 1. Kaplan-Meier plot displaying cumulative incidence of lung cancer development (A) and overall survival (B) in IPF patients with and without statin use. IPF = idiopathic pulmonary fibrosis, K-M = Kaplan-Meier.

Table 2. Comparison of clinical outcomes in IPF patients with and without statin use.

	Statin non-user (n = 5810)	Statin user (n = 3372)	*P*-value
Lung cancer development in IPF patients (n = 850)	534 (9.2%)	316 (9.4%)	0.803
Duration (days)			
Lung cancer development	2194.6 ± 1601.4	3361.0 ± 1331.2	< 0.0001
IPF diagnosis to death	2413.9 ±1778.7	3741.8 ± 1443.1	< 0.0001
No. of deaths	3887 (66.9%)	1404 (41.6%)	< 0.0001

Özet

- İPF hastalarında akciğer kanseri gelişme riski yüksek
- Kanser varlığı mortaliteyi artırır
- Hastaların tanı ve tedavisi planlanırken akut atak gelişme riski akılda tutulmalıdır
- Her hasta multidisipliner olarak değerlendirilmeli ve şahsa özgü tedavi planlanmalıdır

Sabrınız için teşekkürler.....