Fibrose Pulmonar Idiopática

O papel fundamental da MGF no diagnóstico precoce

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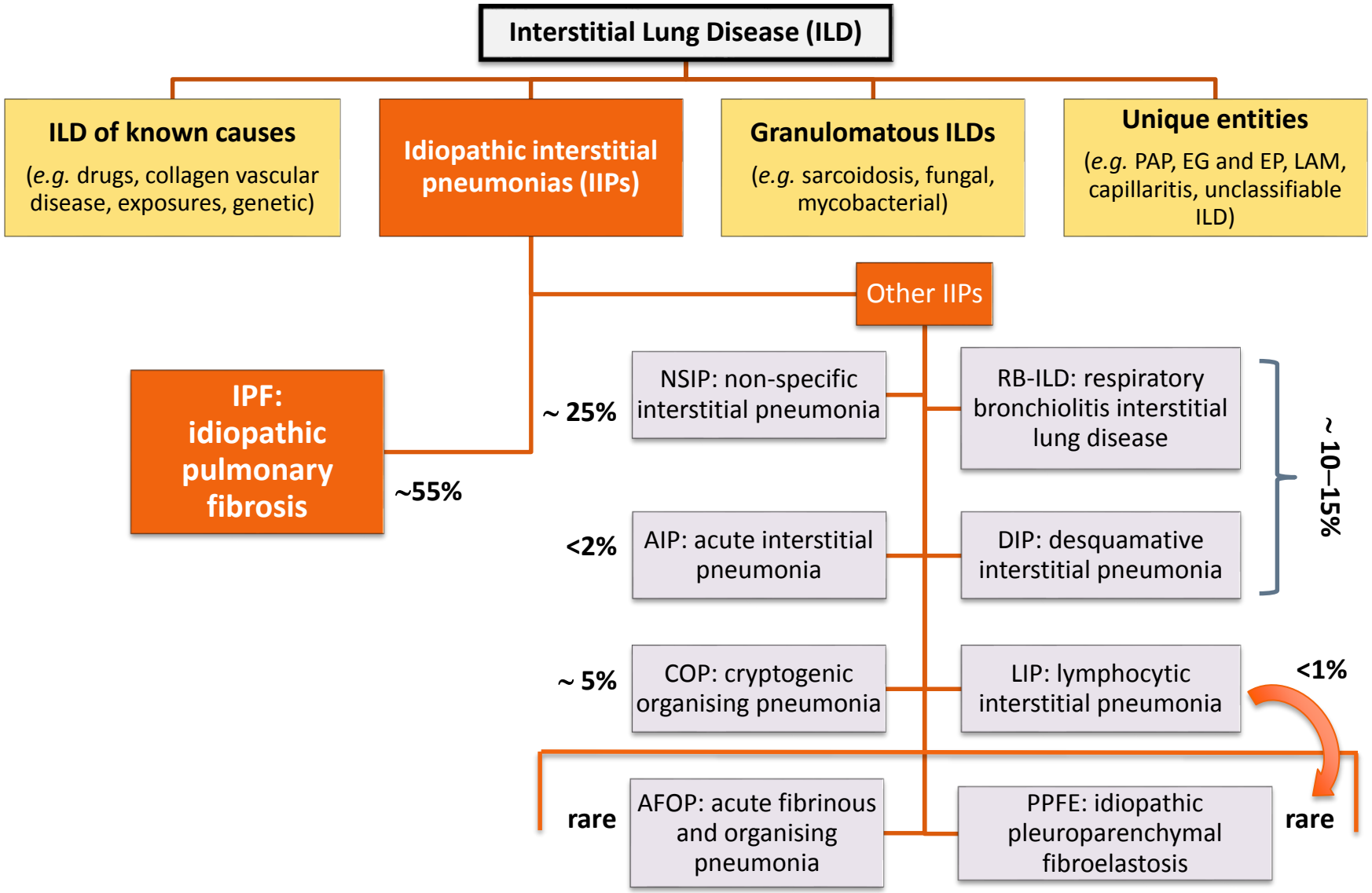
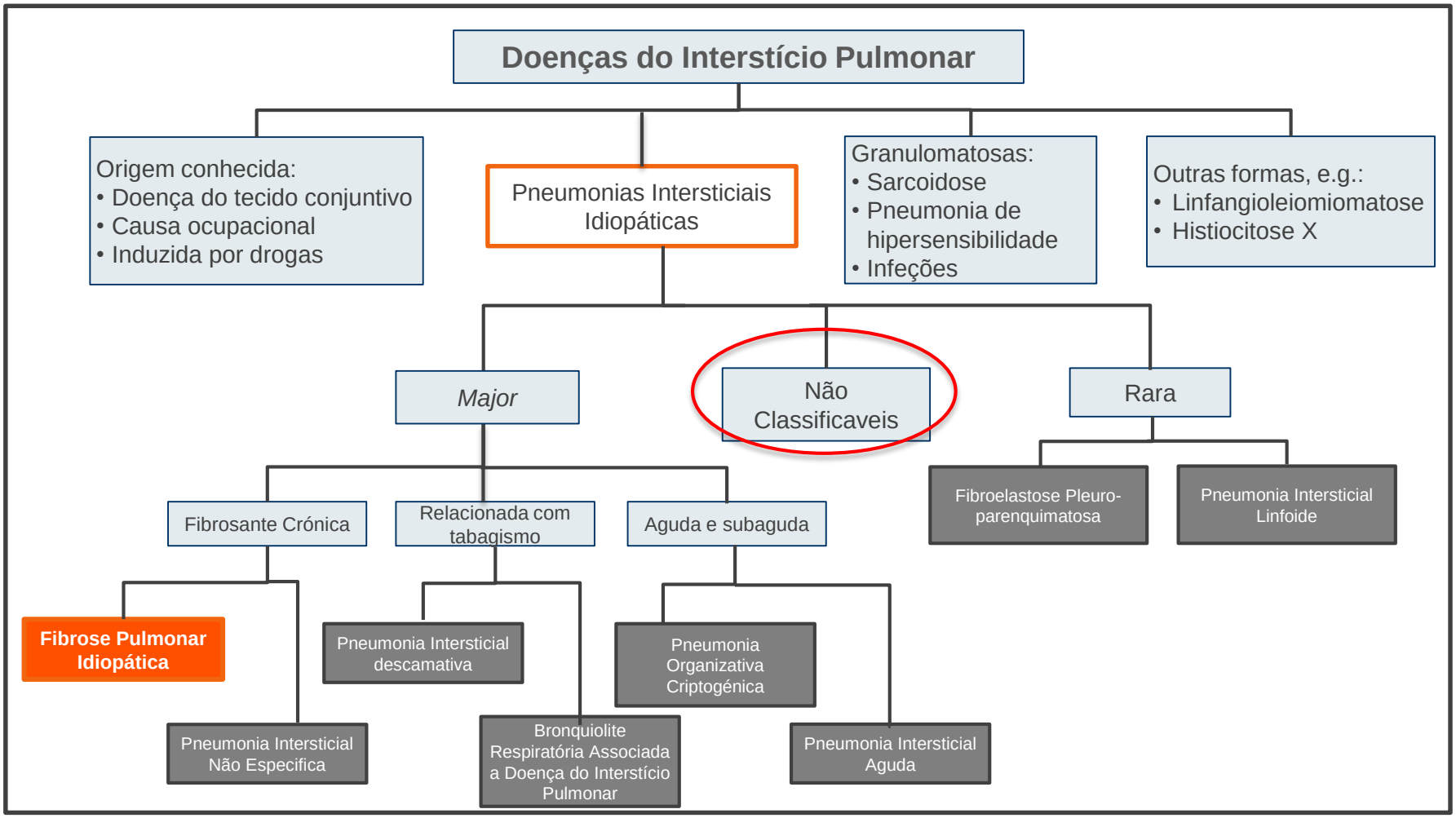

Interstitial Lung Disease (ILD)
ILD of known causes
(e.g. drugs, collagen vascular disease, exposures, genetic)
Idiopathic interstitial pneumonias (IIPs)
Granulomatous ILDs
(e.g. sarcoidosis, fungal, mycobacterial)
Unique entities
(e.g. PAP, EG and EP, LAM, capillaritis, unclassifiable ILD)
Other IIPs
IPF: idiopathic pulmonary fibrosis
~55%
~ 25%
NSIP: non-specific interstitial pneumonia
RB-ILD: respiratory bronchiolitis interstitial lung disease
~ 10–15%
<2%
AIP: acute interstitial pneumonia
DIP: desquamative interstitial pneumonia
~ 5%
COP: cryptogenic organising pneumonia
LIP: lymphocytic interstitial pneumonia
<1%
rare
AFOP: acute fibrinous and organising pneumonia
PPFE: idiopathic pleuroparenchymal fibroelastosis
rare

Doenças Pulmonares Intersticiais



ATS and ERS. Am J Respir Crit Care Med 2002;165:277–304; ATS and ERS. Am J Respir Crit Care Med 2013;188:733–748.

Prevalence and prognosis of unclassifiable interstitial lung disease

Christopher J. Ryerson[1], Thomas H. Urbania[2], Luca Richeldi[3], Joshua J. Mooney[4], Joyce S. Lee[4], Kirk D. Jones[5], Brett M. Elicker[2], Laura L. Koth[4], Talmadge E. King Jr[4], Paul J. Wolters[4] and Harold R. Collard[4]

ABSTRACT The aim of this study was to determine the prevalence, characteristics and outcomes of patients with unclassifiable interstitial lung disease (ILD) and to develop a simple method of predicting disease behaviour.

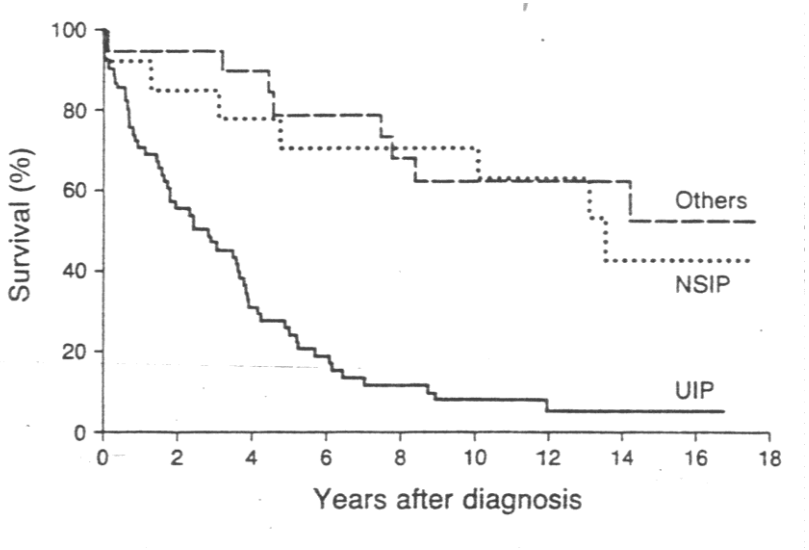
Unclassifiable ILD patients were identified from an ongoing longitudinal cohort. Unclassifiable ILD was diagnosed after a multidisciplinary review did not secure a specific ILD diagnosis. Clinical characteristics and outcomes were compared with idiopathic pulmonary fibrosis (IPF) and non-IPF ILDs. Independent predictors of mortality were determined using Cox proportional-hazards analysis to identify subgroups with distinct disease behaviour.

Unclassifiable ILD was diagnosed in 10% of the ILD cohort (132 out of 1370 patients). The most common reason for being unclassifiable was missing histopathological assessment due to a high risk of surgical lung biopsy. Demographic and physiological features of unclassifiable ILD were intermediate between IPF and non-IPF disease controls. Unclassifiable ILD had longer survival rates when compared to IPF on adjusted analysis (hazard ratio 0.62, p=0.04) and similar survival compared to non-IPF ILDs (hazard ratio 1.54, p=0.12). Independent predictors of survival in unclassifiable ILD included diffusion capacity of the lung for carbon monoxide (p=0.001) and a radiological fibrosis score (p=0.02).

Unclassifiable ILD represents approximately 10% of ILD cases and has a heterogeneous clinical course, which can be predicted using clinical and radiological variables.

Eur Respir J 2013; 42: 750-757

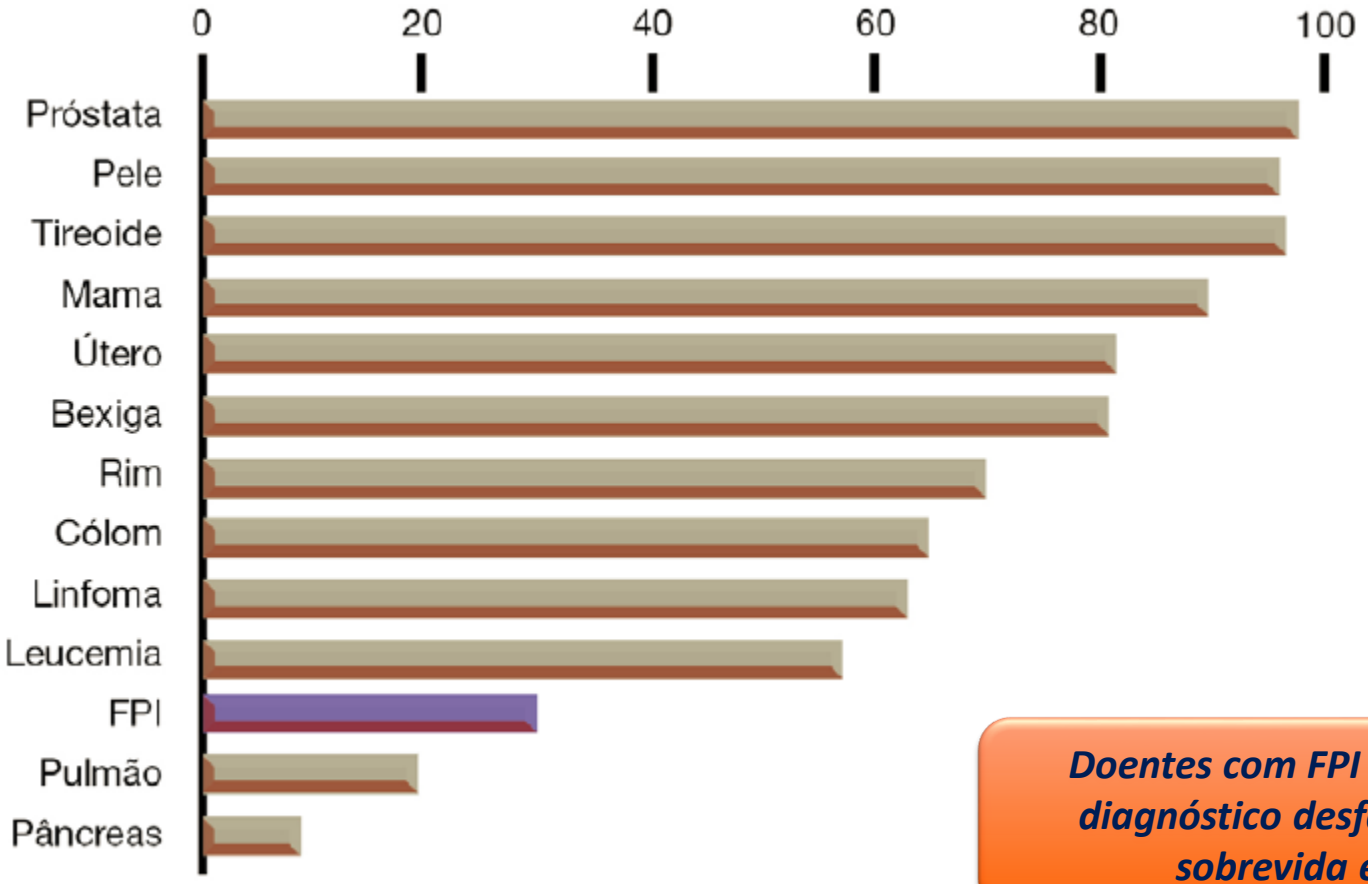
IPF SURVIVAL



Bjoraker JA et al. AJRCCM 1998

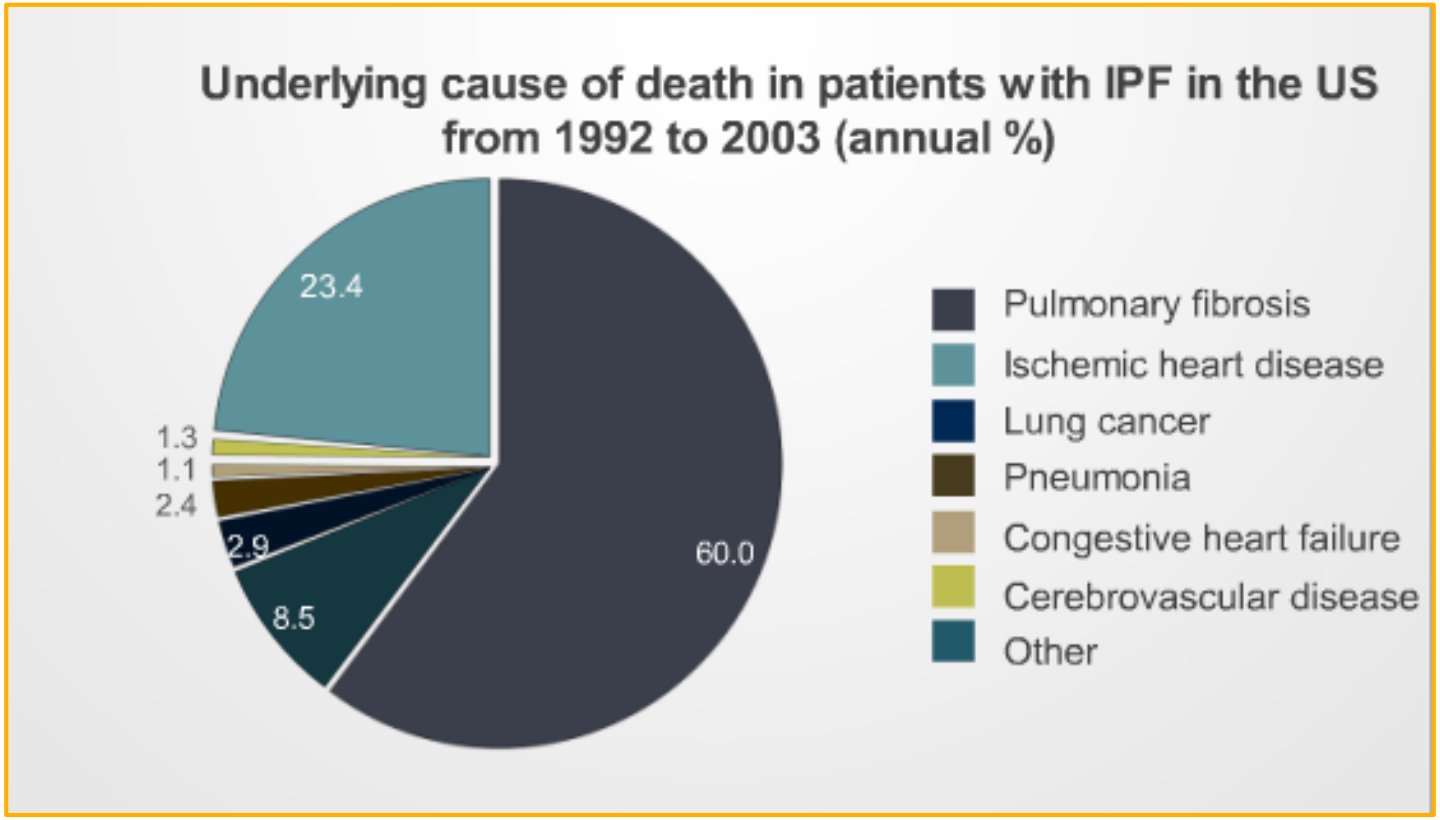
Progressão Clínica da FPI

- **Sobrevida em 5 anos (%)**



Doentes com FPI possuem um diagnóstico desfavorável e a sobrevida é baixa

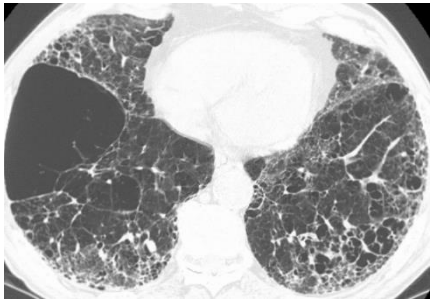
Primary cause of death in patients with IPF



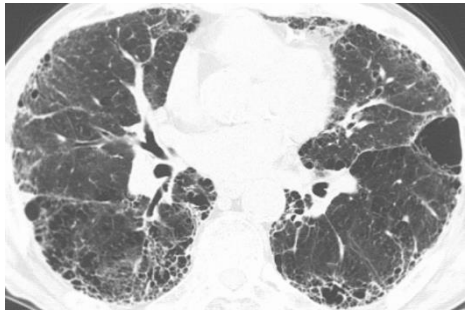
Olson AL, et al. Am J Respir Crit Care Med 2007;176:277–284.

♂ 75 anos, 80 UMA

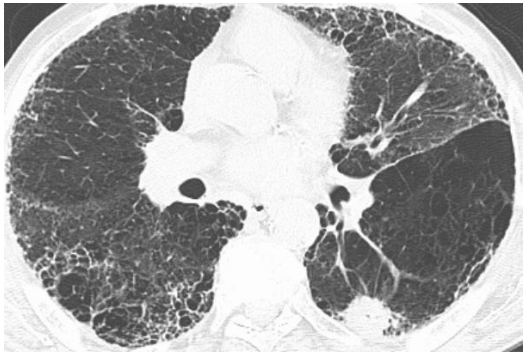
DPOC com Enfisema



Fibrose pulmonar



Carcinoma



Incidência e Prevalência da FPI

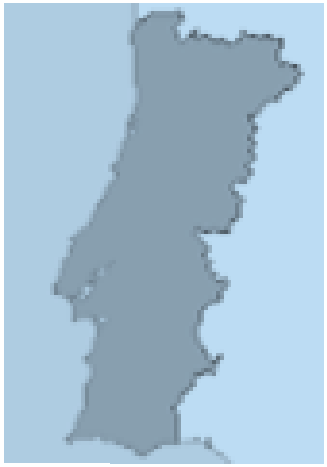
Período do Estudo	Idade do Doente	Local do Estudo	Taxa de incidência 100 000 pessoas-ano	Prevalência por 100 000
1991–2003	>40 anos no diagnóstico	Reino Unido	4.6[1]	—
2000–2008	>40 anos no diagnóstico	Reino Unido	7.4[2]	—
1996–2000	≥18 anos	EUA	6.8–16.3*[3]	14.0–42.7*
1997–2005	≥50 anos	EUA	8.8–17.4*[4]	27.9–63.0*

*Segundo definição restrita ou ampla

1. Gribbin J, et al. Thorax 2006;61:980–985; 2. Navaratnam V, et al. Thorax 2011;66:462–467;
3. Raghu G, et al. Am J Respir Crit Care Med 2006;174:810–816; 4. Fernandez Perez ER, et al. Chest 2010;137:129–137.

A FPI é frequente?

A FPI está classificada como uma doença rara

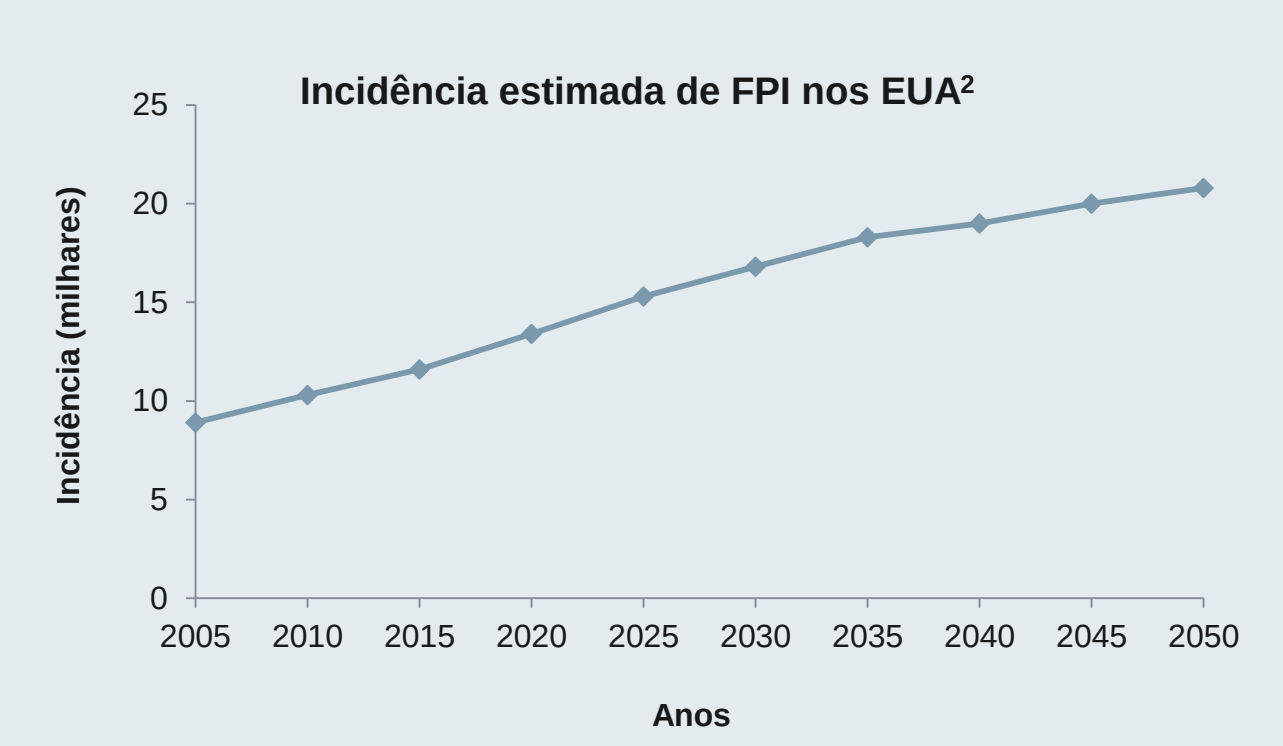


?

doentes

Incidência a aumentar

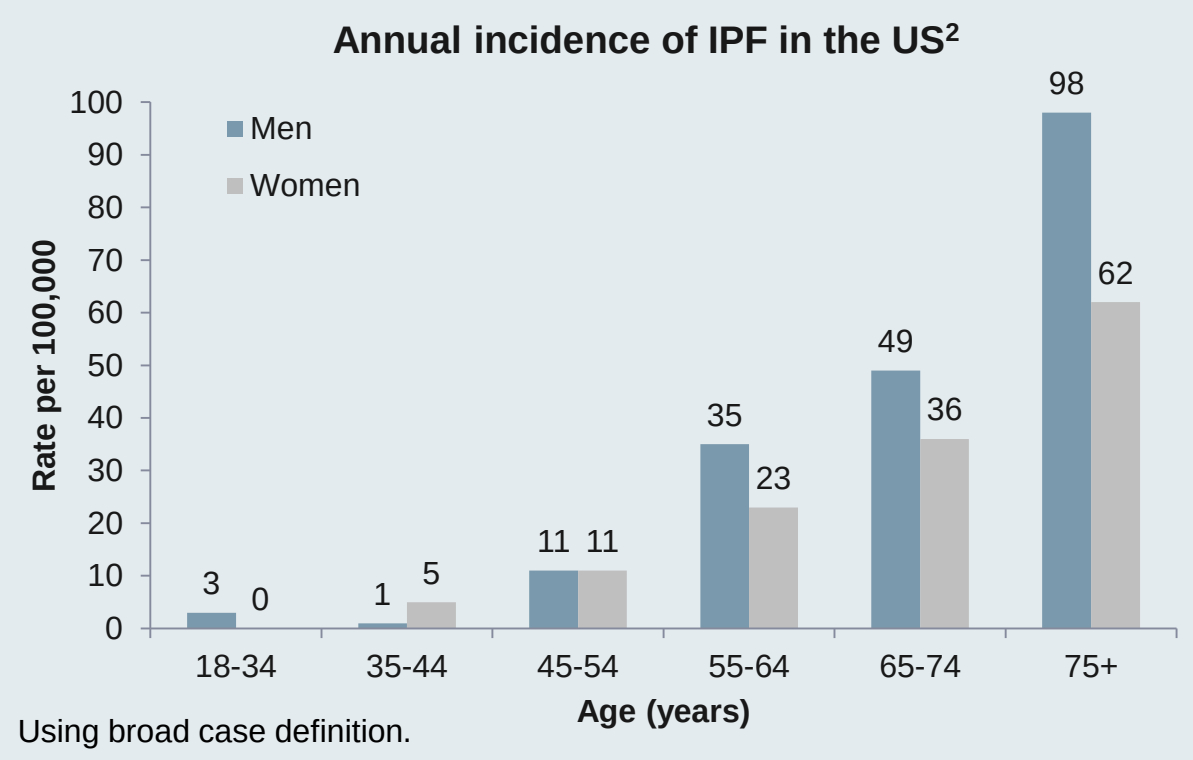
- Estima-se um aumento do número de novos casos de FPI[1,2]



1. Gribbin J, et al. Thorax 2006;61:980–985; 2. Fernandez Perez ER, et al. Chest 2010;137:129–137.

Demographic factors affecting incidence of IPF

- The incidence of IPF increases with age, and is generally higher in men than women[1,2]



Using broad case definition.

1. Meltzer EB and Noble PW. Orphanet J Rare Dis 2008;3:8;
2. Raghu G, et al. Am J Respir Crit Care Med 2006;174:810–816.

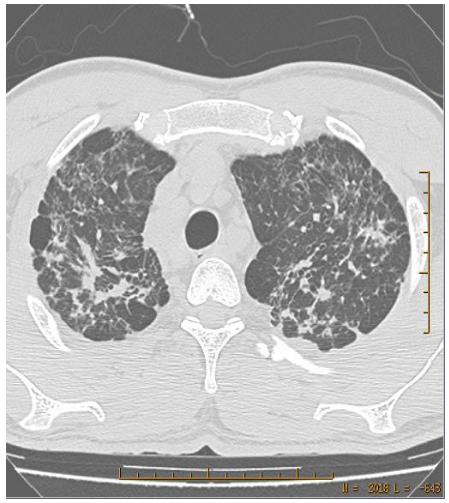
IPF: risk factors and possible aetiologies

Although the cause of IPF is unknown, several risk factors have been suggested

Environmental factors

Cigarette smoking
Strongly associated with IPF

Especially in people with a smoking history of >20 pack-years



Environmental pollutants
Associated with an increased risk of IPF

Exposure to metal and wood dusts, farming, raising birds, hairdressing, stone cutting/polishing, and exposure to livestock, vegetables or animal dust

Gender and Age

Infection
A large number of studies have examined this, but findings are not conclusive

Gastroesophageal reflux disease (GERD)
Proposed cause of repeated micro-injury

Genetic factors

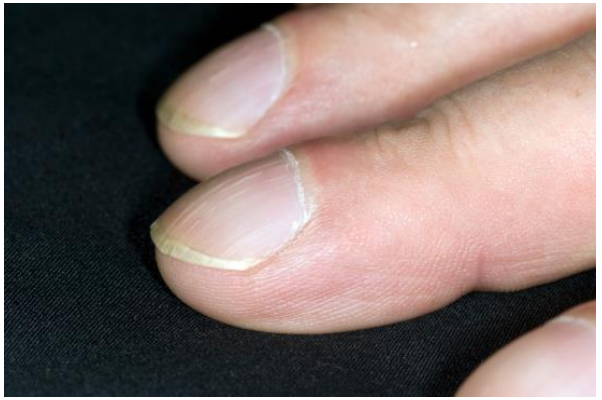
Familial pulmonary fibrosis accounts for <5% of total population with IPF

Principais Sintomas

- Os sintoma mais comuns são **dispneia de esforço** e **tosse seca** [1]
- Os sintomas são frequentemente confundidos com os de doença cardíaca, enfisema, bronquite, asma e DPOC[2]
- **Fervores/Crepitações** inspiratórios “Velcro” ocorrem em >80% dos doentes e podem ajudar ao diagnóstico precoce de FPI [4]
- Hipocratismo digital é observado em 25–50% dos doentes[3,4]

1. Raghu G, et al. Am J Respir Crit Care Med 2011;183:788–824; 2. Collard HR, et al. Respir Med 2007:101:1350–1354; 3. ATS and ERS. Am J Respir Crit Care Med 2000;161:646–664; 4. Borchers AT, et al. Clin Rev Allergy Immunol 2011;40:117–134.

Diagnóstico de IPF



The typical IPF patient

- Over 45 years old
- Smoker or ex-smoker
- Male > female
- Exertional dyspnoea usually present for more than 6 months
- Dry, non-productive cough
- Comorbidities[1,2]

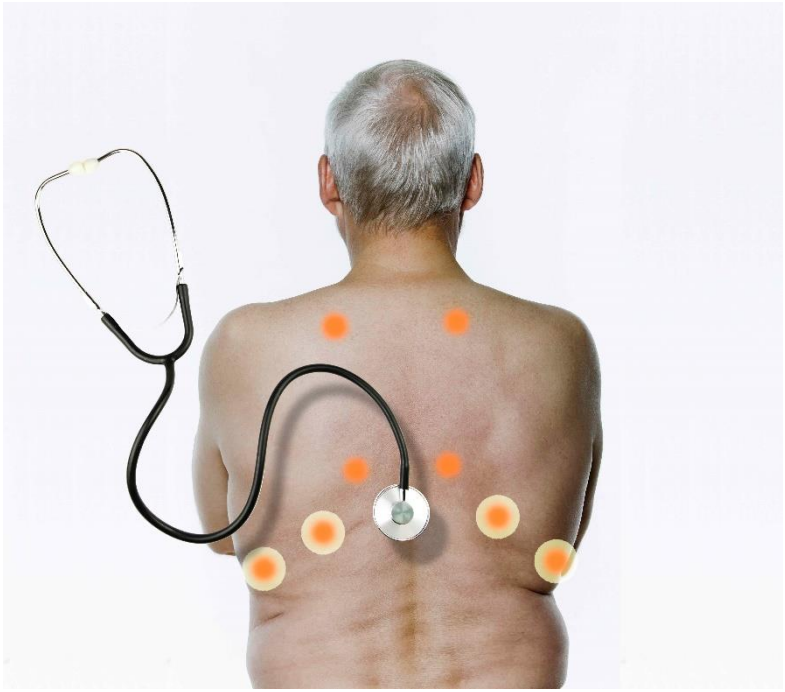
– May include
  - Pulmonary hypertension
  - Gastro-oesophageal reflux
  - Emphysema

– These may be sub-clinical (asymptomatic)

Bibasilar inspiratory crackles may indicate idiopathic pulmonary fibrosis (IPF)

Fine crackles on inspiration are characteristic of IPF

- Similar to the sound heard when gently separating a strip of Velcro
- Predominantly located in the lower, posterior (basal) areas of the lung



Bilateral fine crackles should raise the suspicion of IPF and prompt referral for pulmonary function tests prior to a thin-slice HRCT scan without contrast agent

Cottin V, Cordier J-F. Eur Respir J. 2012;40:519-21

Neglected evidence in idiopathic pulmonary fibrosis: from history to earlier diagnosis

Jean-François Cordier and Vincent Cottin

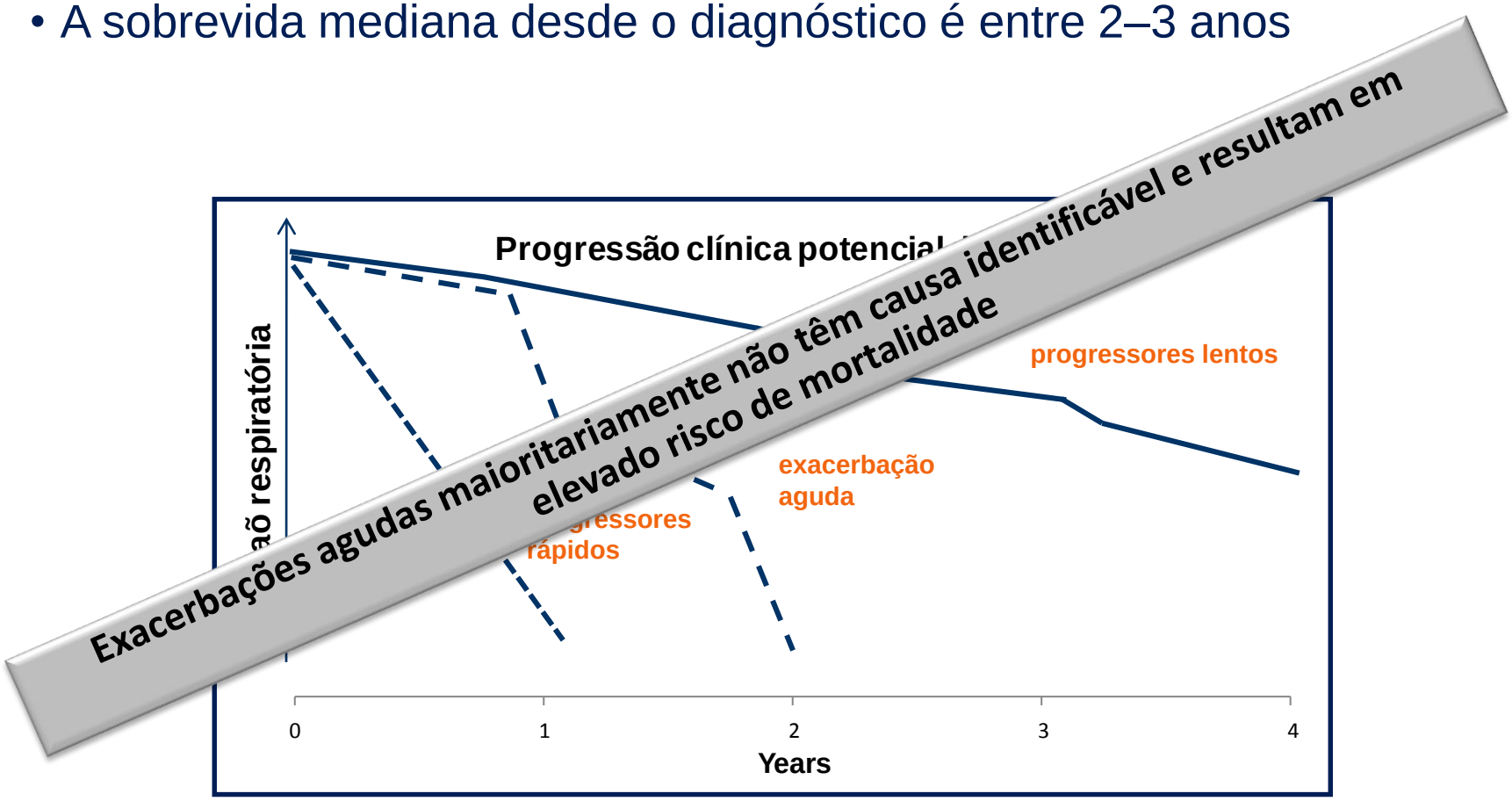
ABSTRACT This perspective highlights some evidence that has hitherto been neglected, especially because it may not have been sufficiently explicated in the clinical respiratory medicine literature. Idiopathic pulmonary fibrosis (IPF) has appeared only in the second half of the 20th century and, like lung cancer and chronic obstructive pulmonary disease, may be a direct consequence of the cigarette smoking epidemic. It is a disease of lung ageing, with most affected patients being >70 years of age. The relationship between lung ageing and pulmonary fibrosis is further illustrated in the bleomycin mouse model, in which older males develop more fibrosis than young female mice.

Earlier diagnosis of IPF is a prerequisite for significant progress to be made in the long-term outcome and prognosis. We consider that only two different yet complementary and realistic approaches could lead to earlier diagnosis of IPF and possibly to allowing more efficient disease management: 1) investigating any patients with early Velcro crackles at lung auscultation through proactive education of, and commitment from, primary care physicians; and 2) using current large-scale lung cancer screening strategies with low-dose high-resolution computed tomography in smokers for the detection of subclinical interstitial lung disease and especially early IPF.

Eur Respir J 2013; 42: 916-923

Progressão Clínica da FPI

- A progressão clínica da FPI é heterogénea
- A sobrevida mediana desde o diagnóstico é entre 2–3 anos



Ley B, et al. Am J Respir Crit Care Med 2011;183:431–440; Raghu G, et al. Am J Respir Crit Care Med 2011;183:788–824; Kim DS, et al. Proc Am Thorac Soc 2006;3:285–292.

IPF disease progression is inevitable yet unpredictable

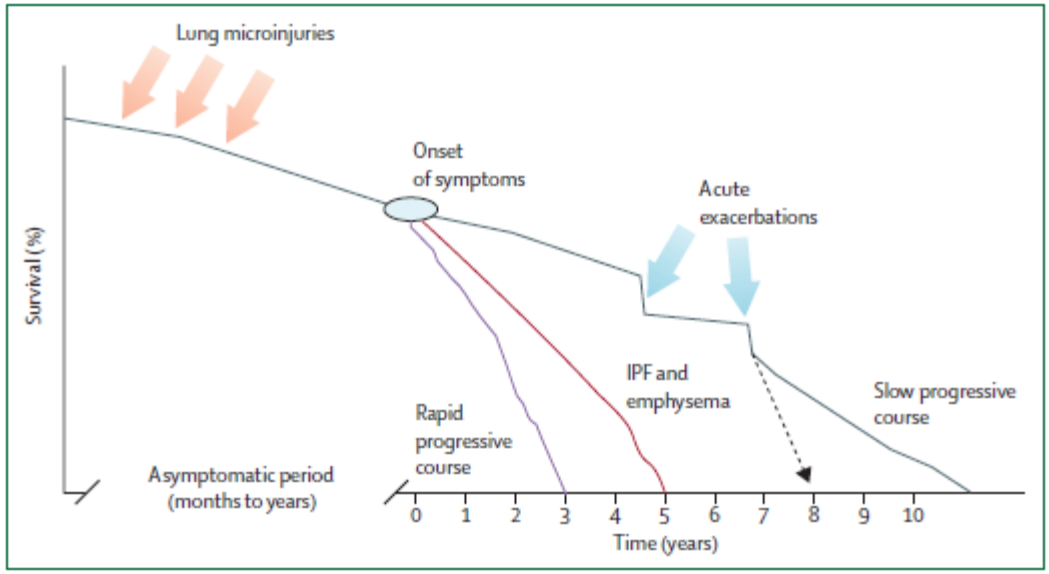
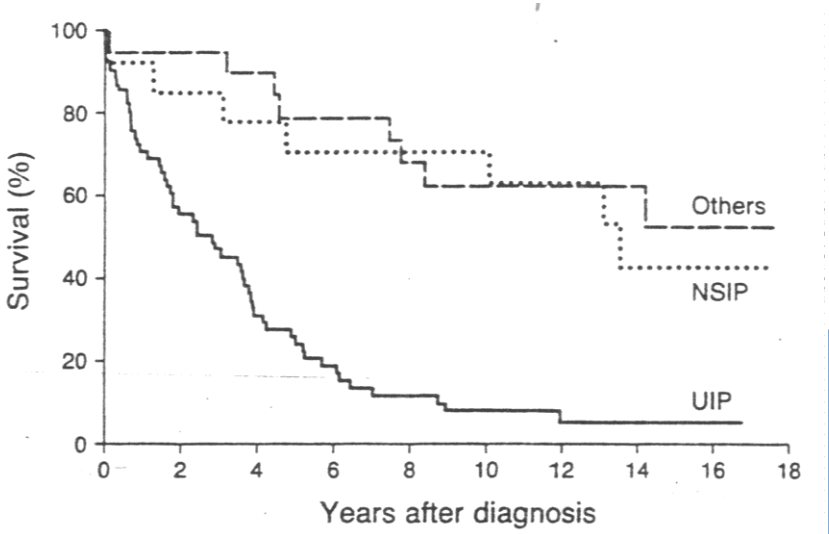


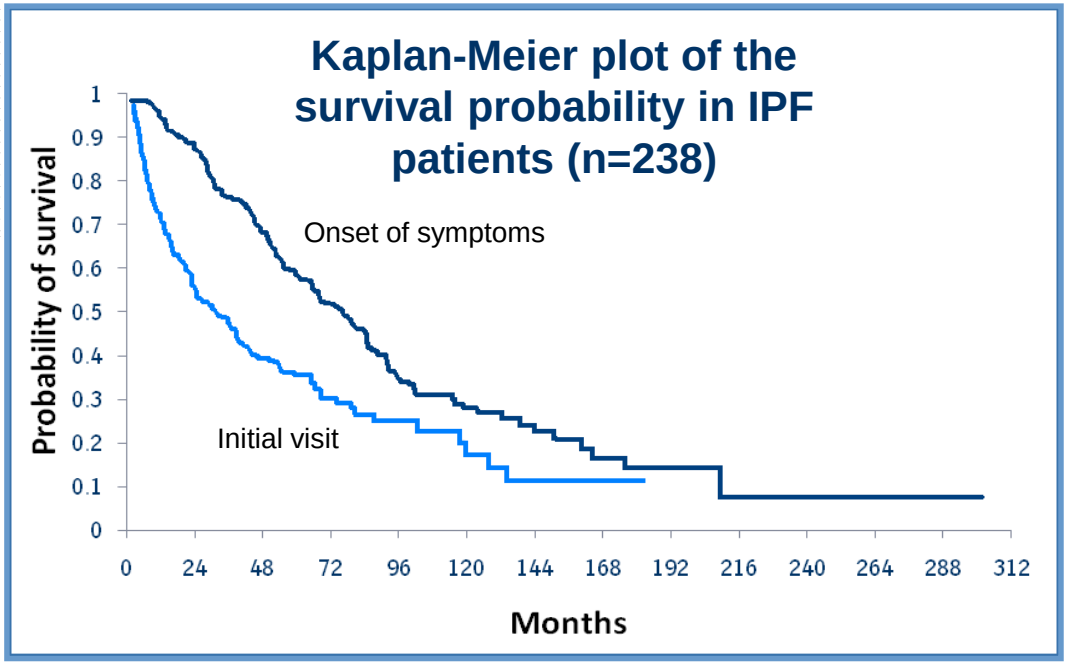
Figure 2: **Clinical phenotypes of IPF**
The heterogeneous natural history pattern in patients with IPF. The disease has a long (months to years) asymptomatic period. Patients consult when the severity of the lung lesions reaches a threshold that is enough to provoke symptoms. Most patients follow a relatively slow clinical and functional decline (slowly progressive) after diagnosis. About 10% of these patients present with episodes of acute clinical deterioration (acute exacerbations) that precede and possibly initiate the terminal phase of their disease. A few patients have a short duration of illness with a rapidly progressive clinical course. Heavy smokers might develop pulmonary fibrosis combined with emphysema, with shorter survival compared with patients with IPF alone. IPF=idiopathic pulmonary fibrosis.

King T, Pardo A, Selman M. Idiopathic Pulmonary Fibrosis. Lancet 2011;378:1949-1961

IPF: survival

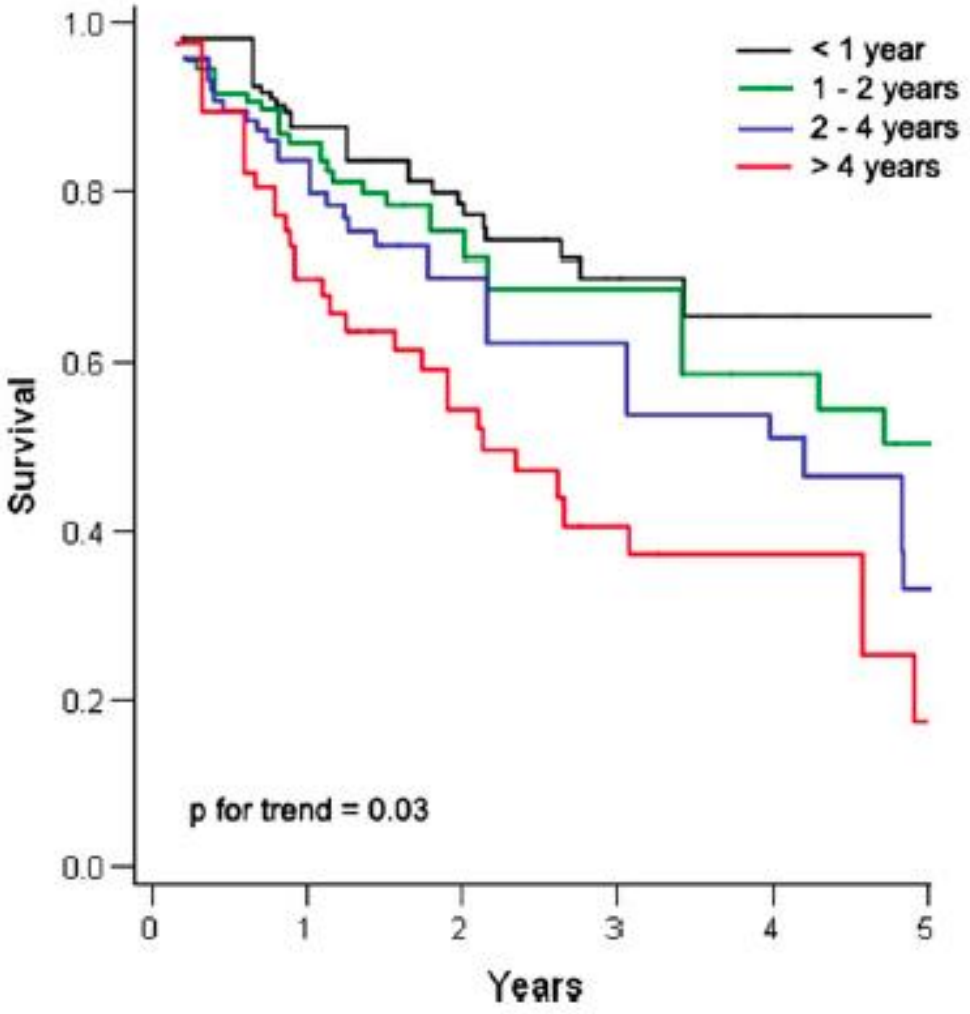


Bjoraker JA et al. AJRCCM 1998



Adapted from King et al. 2001

Survival from the time of evaluation at a tertiary care center adjusted for age and FVC across quartiles of delay



Entry time into the cohort began at study enrollment

Am J Respir Crit Care Med Vol 184. pp 842–847, 2011

When and where to refer

The patient should be referred to a pulmonologist if the following are noted:

- Progressive breathlessness on exertion ≥3 months
- Dry cough ≥3 months
- Basal inspiratory crackles on auscultation
- Over 45 years old

ATS/ERS/JRS/ALAT. Am J Respir Crit Care Med 2011;183:788-824

The importance of early recognition and referral

Early identification of idiopathic pulmonary fibrosis (IPF) is important:

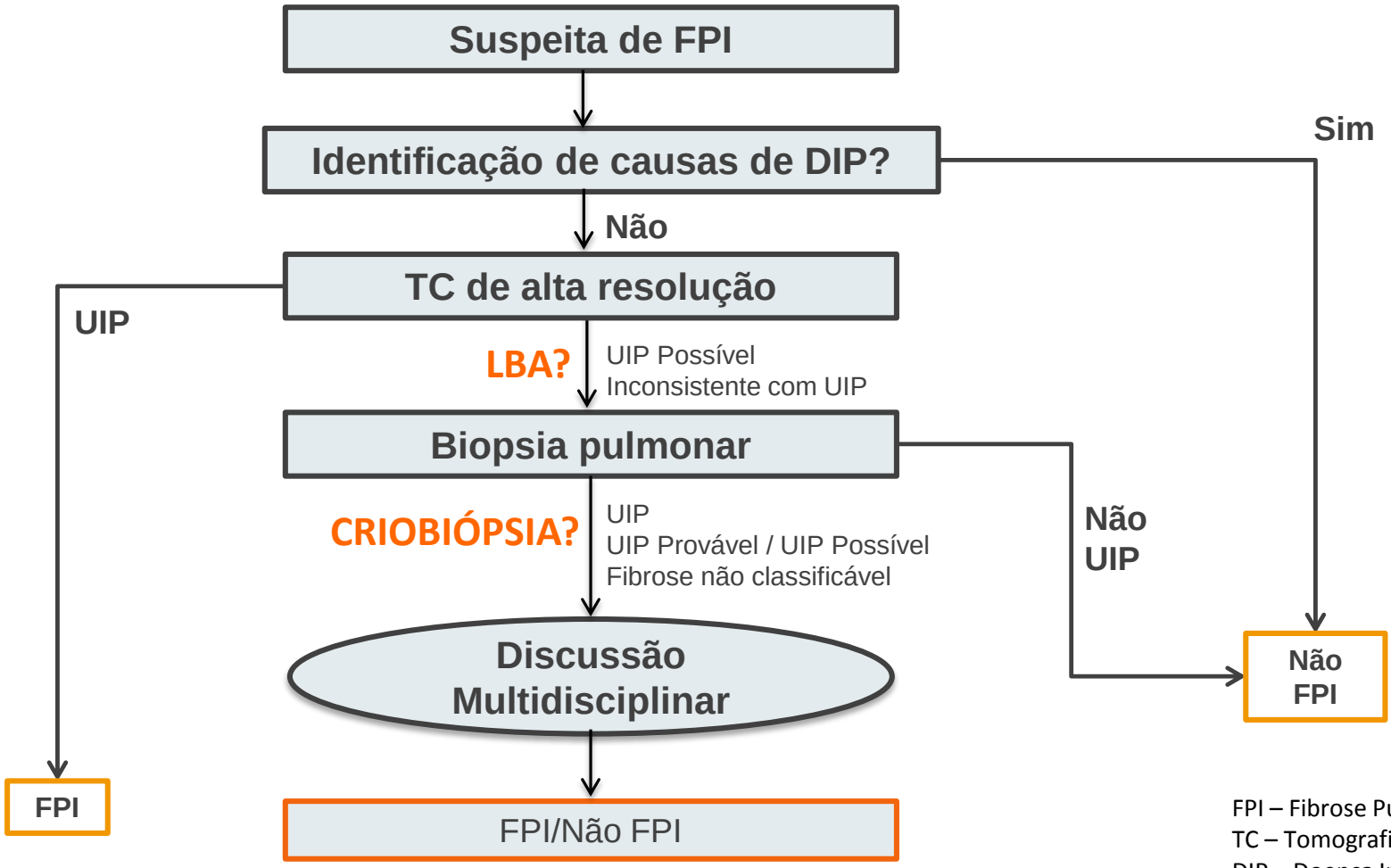
- To confirm diagnosis and ensure timely referral[1]
- Because effective treatment to slow disease progression is available[2]
  - Early intervention may improve outcomes
- To list for lung transplant[2]
- Because there are several ongoing trials for potential new therapies[3]
- To give patients the opportunity to make the most of their remaining time

1.ATS/ERS. Am J Respir Crit Care Med 2002;165:277-304

2.ATS/ERS/JRS/ALAT. Am J Respir Crit Care Med 2011;183:788-824

3.Available at www.clinicaltrials.gov [Accessed May 2013]

Algoritmo de Diagnóstico



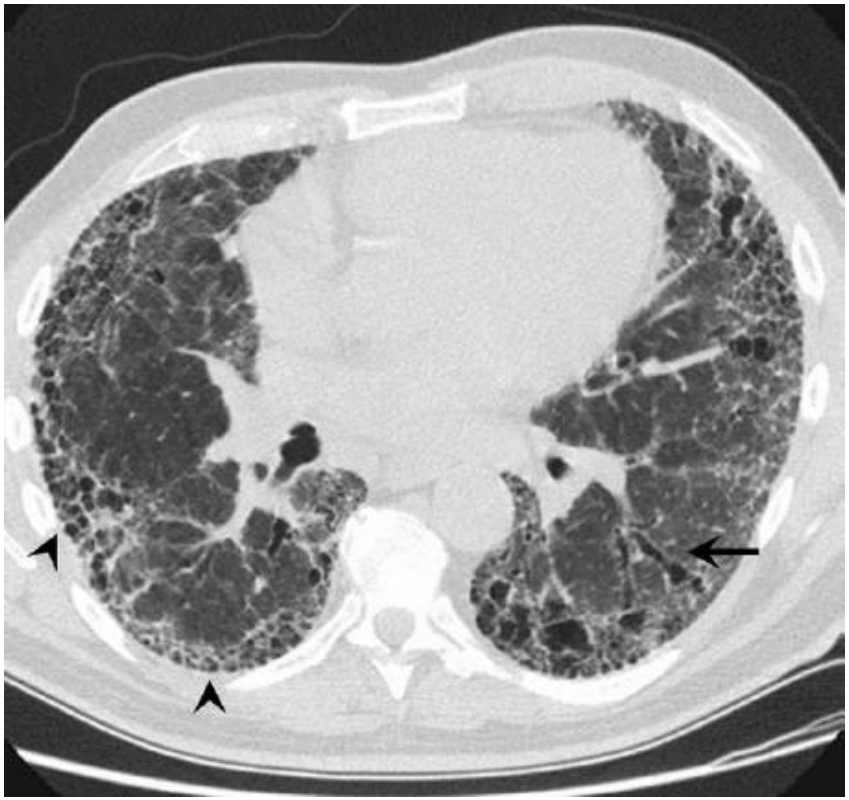
Raghu G, et al. Am J Respir Crit Care Med 2011;183:788–824.

FPI – Fibrose Pulmonar Idiopática
TC – Tomografia Computorizada
DIP – Doença Intersticial Pulmonar
UIP – Usual interstitial pneumonia (pneumonia intersticial usual)

High-resolution computed tomography

- HRCT is an integral component in the diagnosis of IPF
- UIP is characterized on HRCT by:[1]
  - Subpleural, basal predominance
  - Reticular abnormality
  - Honeycombing w/o traction bronchiectasis
  - Absence of features inconsistent with UIP pattern
- Detection of a UIP pattern in HRCT is highly accurate for the presence of UIP pattern in surgical lung biopsy[1]

HRCT scan of a patient with IPF



Adapted from Meltzer and Noble 2008[2]

1. Raghu G, et al. Am J Respir Crit Care Med 2011;183:788–824;
2. Meltzer EB and Noble PW. Orphanet J Rare Dis 2008;3:8.

HRCT criteria for UIP pattern

UIP pattern (all features)	Possible UIP pattern (all features)	Inconsistent with UIP pattern (any of these features)
• Subpleural, basal predominance • Reticular abnormality • Honeycombing w/o bronchiectasis • Absence of 'inconsistent' features with UIP	• Subpleural, basal predominance • Reticular abnormality • Absence of 'inconsistent' features with UIP	• Upper or mid-lung predominance • Peribronchovascular predominance • Extensive ground glass abnormality (extent >reticular abnormality) • Profuse micronodules (bilateral, predominantly upper lobes) • Discrete cysts (multiple, bilateral, away from areas of honeycombing) • Diffuse mosaic attenuation/air-trapping (bilateral, in ≥3 lobes) • Consolidation in bronchopulmonary segment(s)/lobe(s)

Raghu G, et al. Am J Respir Crit Care Med 2011;183:788–824.

Functional tests in IPF

- IPF is a ***restrictive*** lung disease[1,2]
  - Inspiratory capacity is impaired, limiting lung expansion

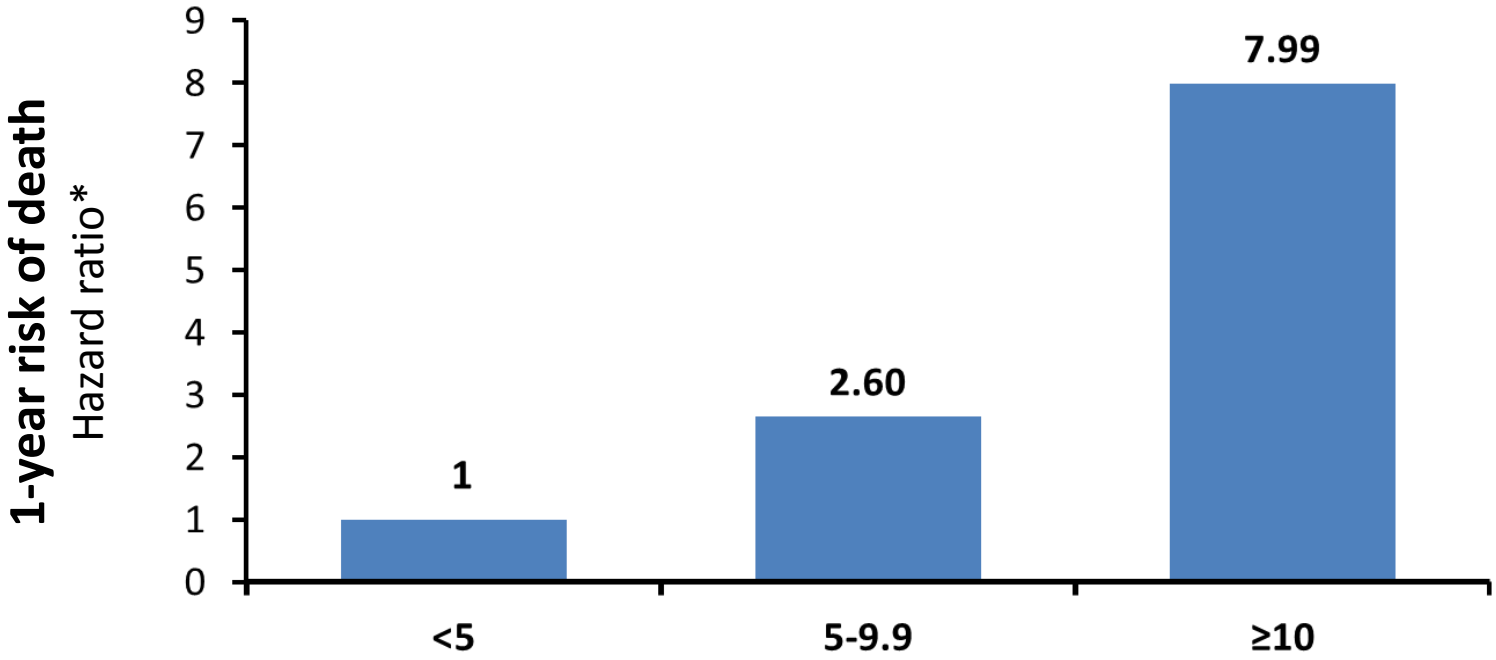
Functional test	Criteria for mild to moderate IPF
% predicted FVC	≥50%
6MWD	≥150 m
% predicted haemoglobin-corrected DLco	> 30–35%

6MWD, 6-minute walk test distance; DLco, diffusing capacity of the lung for carbon monoxide; FVC, forced vital capacity

1. American Thoracic Society/European Respiratory Society. AJRCCM 2002;165:277–304.
2. Meltzer EB and Noble PW. Orphanet J Rare Dis 2008;3:8–22.

FVC as a consistent predictor of mortality in IPF

Categorical decline in FVC of 10% or more in a 6-month period is a consistent predictor of mortality in IPF



*Hazard ratio compared with patients whose % FVC declined by <5%

Adapted from du Bois RM et al. Am J Respir Crit Care Med 2011; 184:459–466.

FVC – the minimal clinically important difference

FVC is a reliable, valid and responsive measure of disease status in patients with IPF

The **minimal clinically important difference** (MCID) is the smallest difference in a measure that may be perceived to be important, either beneficial or harmful, and that would lead a clinician to consider a change in a patient's therapy

Studies suggest that the MCID for percent-predicted FVC is between **2% and 6%**

du Bois RM et al. Am J Respir Crit Care Med 2011; 184:1382–1389

Summary

- IPF is a rare disease characterized by worsening dyspnea and progressive loss of lung function
- A radiological and/or histopathological pattern known as usual interstitial pneumonia (UIP) is essential for the diagnosis of IPF
- The pathogenesis of IPF involves an abnormal wound healing response that ultimately results in scarring and loss of the normal lung architecture
- The clinical course of IPF in an individual patient is impossible to predict
- Decline in FVC is considered a marker of disease progression in patients with IPF
- Acute exacerbations of IPF can occur at any time during the course of disease and are associated with substantial morbidity and mortality

IPF - Goals of Treatment

Stop disease progression

Prolong survival

Prevent acute exacerbations

Reduce symptoms

Treatment of IPF

- Treatment guidelines from the ATS/ERS/JRS/ALAT issued in 2011 do not support the use of any specific pharmacologic treatment in IPF patients[1]
- There is no consensus on the ideal treatment regimen for IPF
- Treatment approaches have traditionally been based on the belief that IPF is a chronic inflammatory disease[2]
- Following a better understanding of the pathogenesis of IPF, new therapies target the molecular events believed to sustain the fibrotic process in IPF[2]

→ Antifibrotic drugs are attractive candidates for IPF treatment

1. *Raghu G et al. Am J Respir Crit Care Med 2011; 183: 788-824.*
2. *Harari S & Caminati A. Allergy 2010; 65: 537–553.*

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS

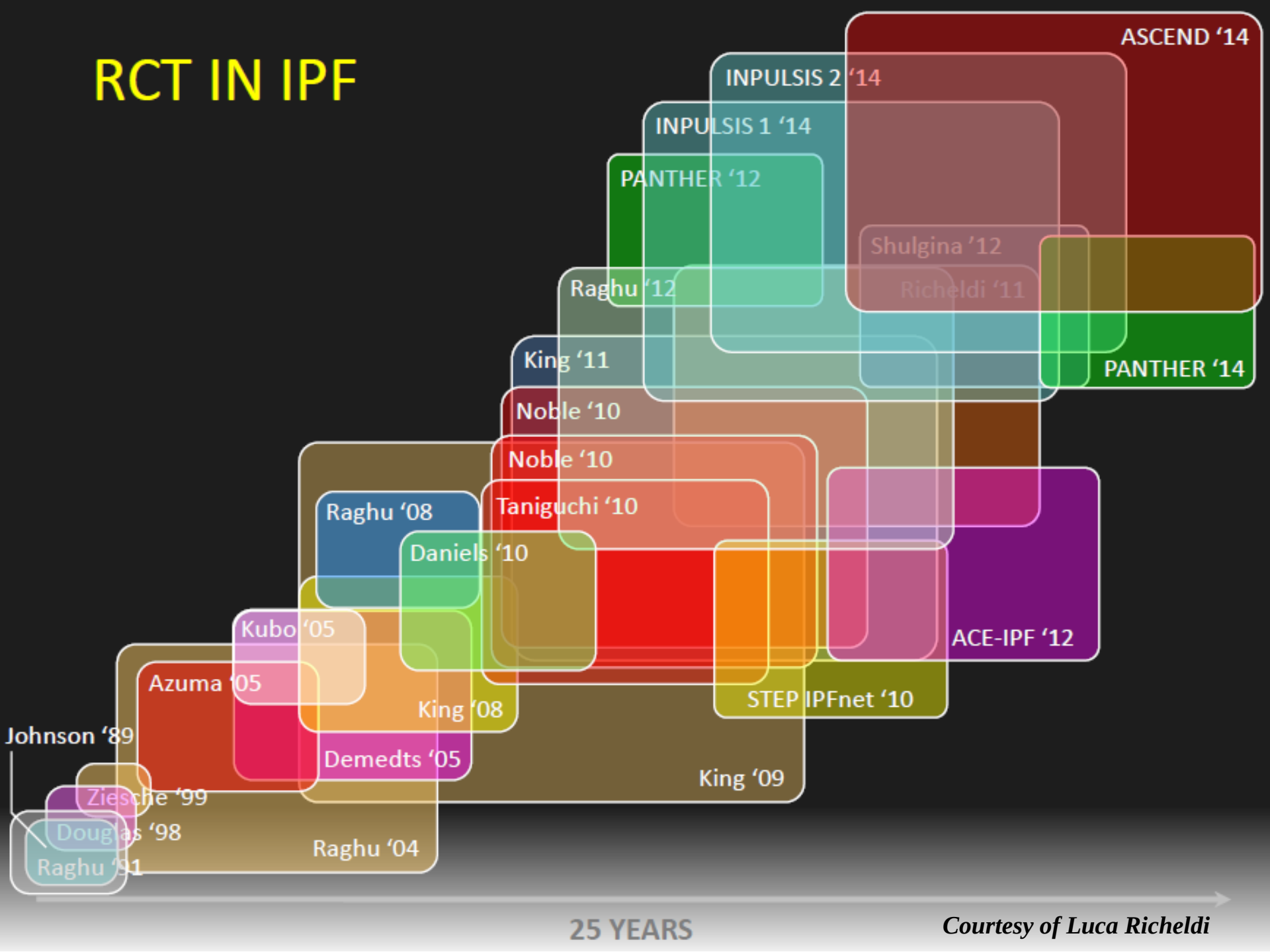
A New Hope for Idiopathic Pulmonary Fibrosis

Gary M. Hunninghake, M.D., M.P.H.

"It is now clear that idiopathic pulmonary fibrosis is a disease perpetuated by aberrant wound healing, rather than primarily by chronic inflammation.

With new understanding comes new hope. As in the 1977 episode of the Star Wars series, the force is finally with us. May we learn to use it wisely."

NEJM 2014; 370: 2142-3


RCT IN IPF
ASCEND '14
INPULSIS 2 '14
INPULSIS 1 '14
PANTHER '12
Shulgina '12
Richeldi '11
Raghu '12
PANTHER '14
King '11
Noble '10
Noble '10
Raghu '08
Taniguchi '10
Daniels '10
ACE-IPF '12
Kubo '05
Azuma '05
King '08
STEP IPFnet '10
Johnson '89
Demedts '05
King '09
Ziesche '99
Douglas '98
Raghu '04
Raghu '91
25 YEARS
Courtesy of Luca Richeldi

An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline: Treatment of Idiopathic Pulmonary Fibrosis

An Update of the 2011 Clinical Practice Guideline

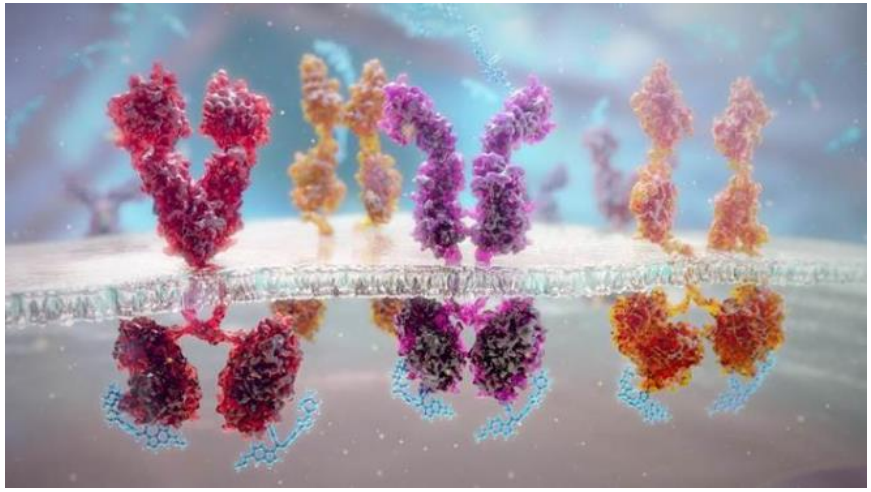
Ganesh Raghu, Bram Rochwerg, Yuan Zhang, Carlos A. Cuello Garcia, Arata Azuma, Juergen Behr, Jan L. Brozek, Harold R. Collard, William Cunningham*, Sakae Homma, Takeshi Johkoh, Fernando J. Martinez, Jeffrey Myers, Shandra L. Protzko, Luca Richeldi, David Rind, Moisés Selman, Arthur Theodore, Athol U. Wells, Henk Hoogsteden, and Holger J. Schünemann; on behalf of the ATS, ERS, JRS, and ALAT

Agent	2015 Guideline	2011 Guideline
New and revised recommendations		
Anticoagulation (warfarin)	Strong recommendation against use*	Conditional recommendation against use‡
Combination prednisone + azathioprine + *N*-acetylcysteine	Strong recommendation against use†	Conditional recommendation against use†
Selective endothelin receptor antagonist (ambrisentan)	Strong recommendation against use†	Not addressed
Imatinib, a tyrosine kinase inhibitor with one target	Strong recommendation against use*	Not addressed
Nintedanib, a tyrosine kinase inhibitor with multiple targets	Conditional recommendation for use*	Not addressed
Pirfenidone	Conditional recommendation for use*	Conditional recommendation against use†
Dual endothelin receptor antagonists (macitentan, bosentan)	Conditional recommendation against use†	Strong recommendation against use*
Phosphodiesterase-5 inhibitor (Sildenafil)	Conditional recommendation against use*	Not addressed
Unchanged recommendations		
Antiacid therapy	Conditional recommendation for use‡	Conditional recommendation for use‡
N-acetylcysteine monotherapy	Conditional recommendation against use†	Conditional recommendation against use†
Antipulmonary hypertension therapy for idiopathic pulmonary fibrosis-associated pulmonary hypertension	Reassessment of the previous recommendation was deferred	Conditional recommendation against use‡
Lung transplantation: single vs. bilateral lung transplantation	Formulation of a recommendation for single vs. bilateral lung transplantation was deferred	Not addressed

Nintedanib: Um inibidor intracelular potente da tirosina quinase

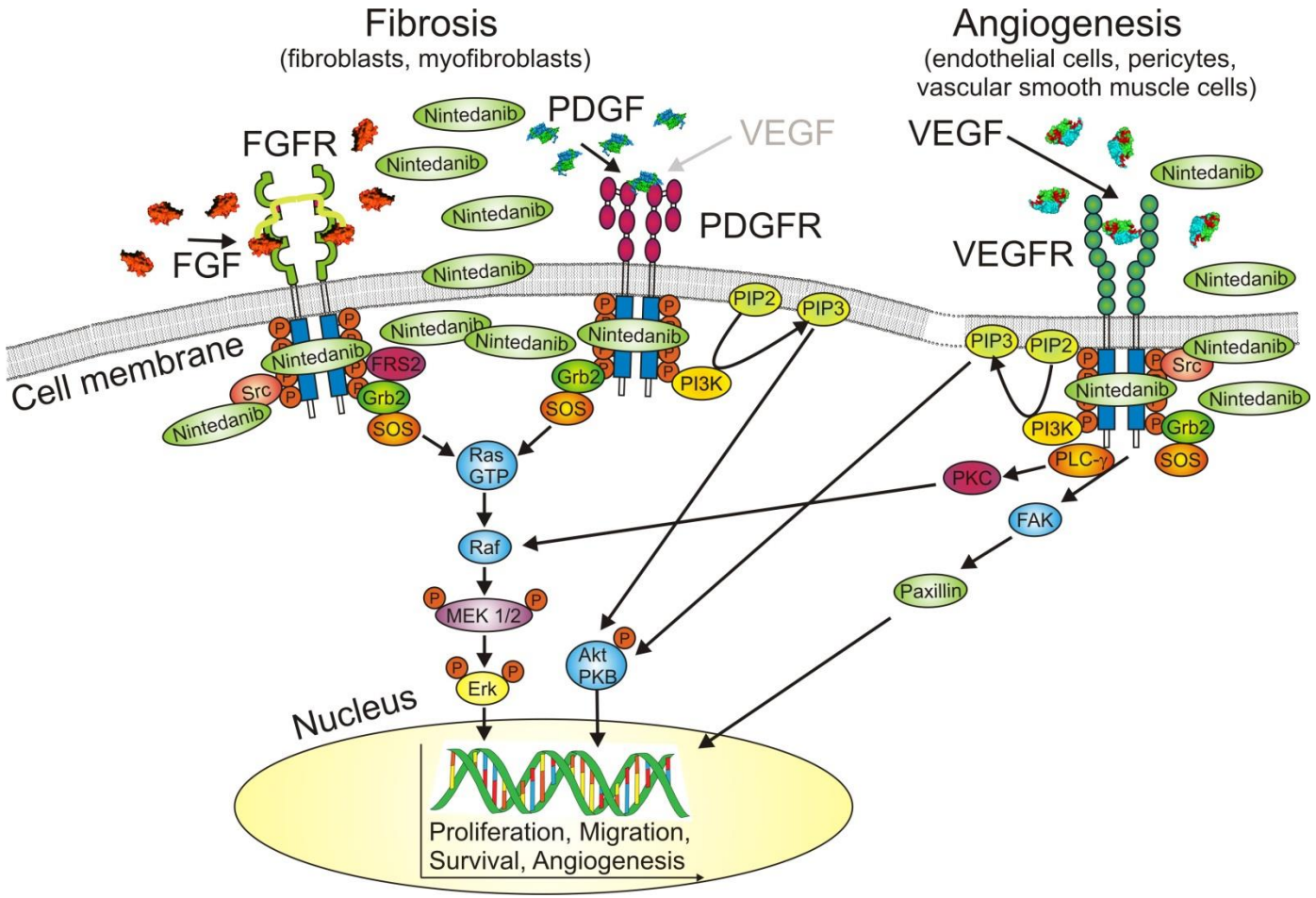
- Nintedanib tem como alvo:
  - fator de crescimento vascular endotelial (VEGF)
  - fator de crescimento derivado de plaquetas (PDGF)
  - fator de crescimento dos fibroblastos (FGF)

- Nintedanib actua através do bloqueio do local de ligação aos receptores e consequente activação e sinalização



Hilberg F, et al. Cancer Res 2008;68:4774–4782; Wollin L, et al. J Pharmacol Exp Ther 2014;349:209–220.

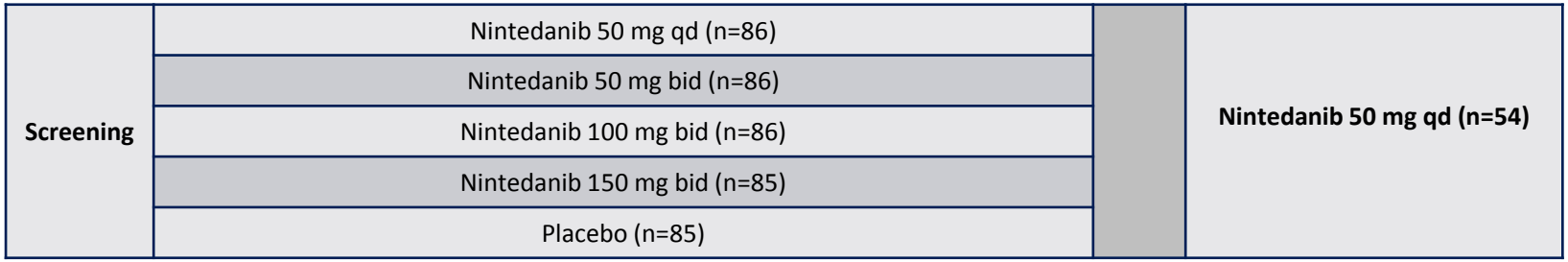
Nintedanib inibe as vias de sinalização envolvidas na patogénese de FPI



Hilberg F, et al. Cancer Res 2008;68:4774–4782; Wollin L, et al. J Pharmacol Exp Ther 2014;349:209–220.

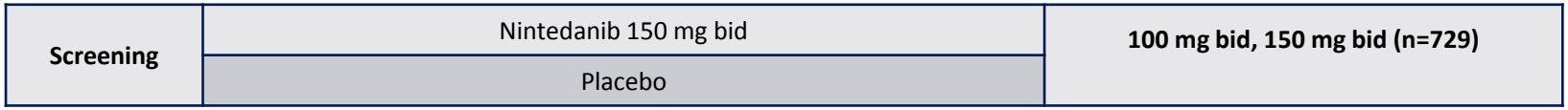
Principais ensaios clínicos de nintedanib em FPI

TOMORROW

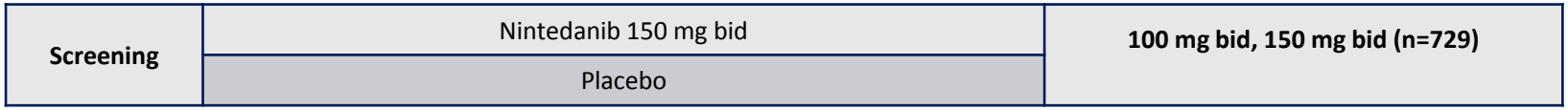


Portugal
6 Centros de investigação
12 doentes recrutados

INPULSIS 1

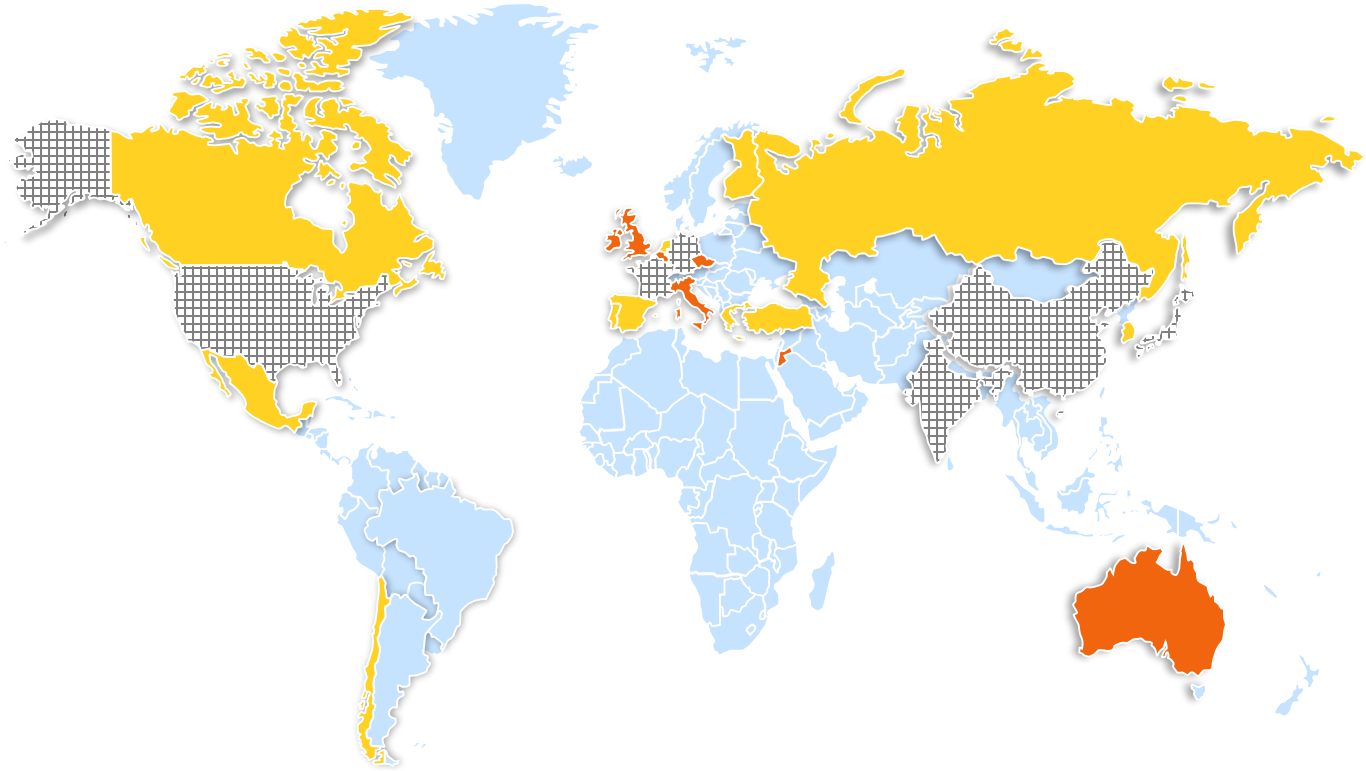


INPULSIS 2



Portugal
5 Centros de investigação
20 doentes recrutados

Países participantes

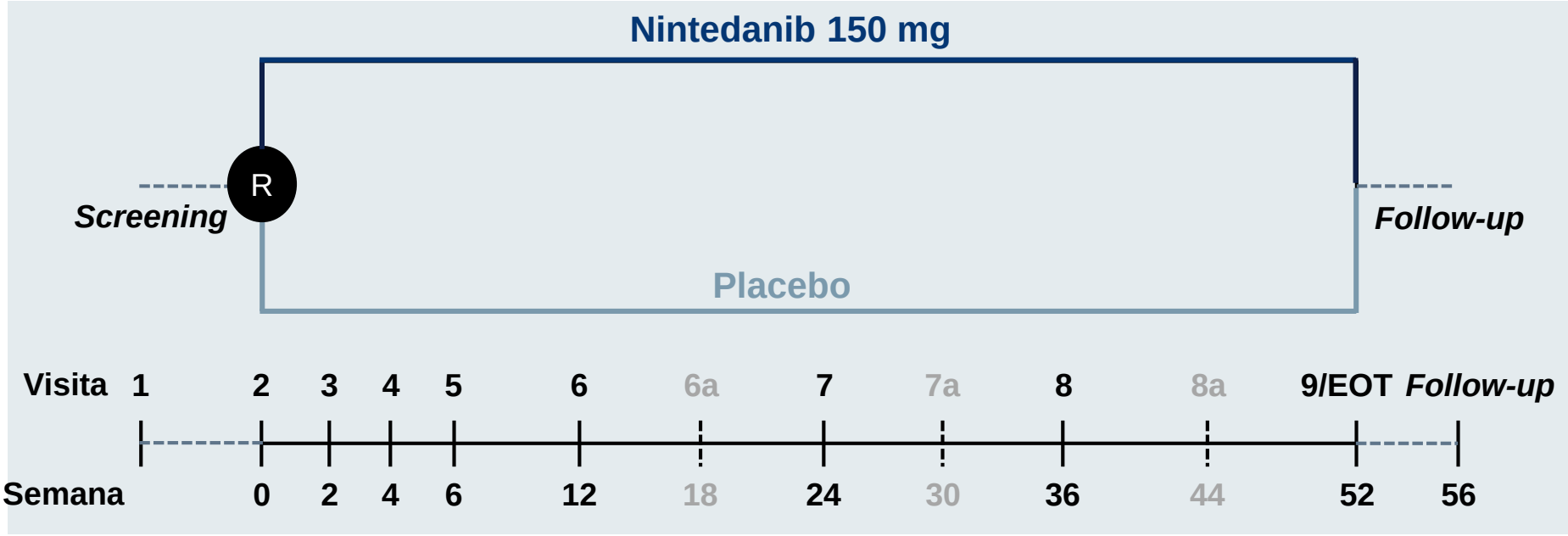


Os ensaios INPULSIS® foram realizados em 205 centros em 24 países

INPULSIS®-1 **INPULSIS®-2** **INPULSIS®-1 e-2**

Richeldi L, et al. N Engl J Med 2014;370:2071–2082; Data on file.

Desenho do Estudo



- Com dupla ocultação, controlados com placebo, fase III
- 52 semanas de tratamento seguidas de 4 semanas de *follow-up*
- Aleatorização com razão 3:2 nintedanib:placebo
- Interrupção de tratamento e/ou diminuição de dose 100 mg bid foi permitida para gestão de acontecimentos adversos

Visits 6a, 7a and 8a were for blood sampling for laboratory tests only. EOT, end of treatment; R, randomization.
Richeldi L, et al. N Engl J Med 2014;370:2071–2082.

Objetivos

Objetivos primário

- Taxa anual de declínio de FVC (mL/ano)

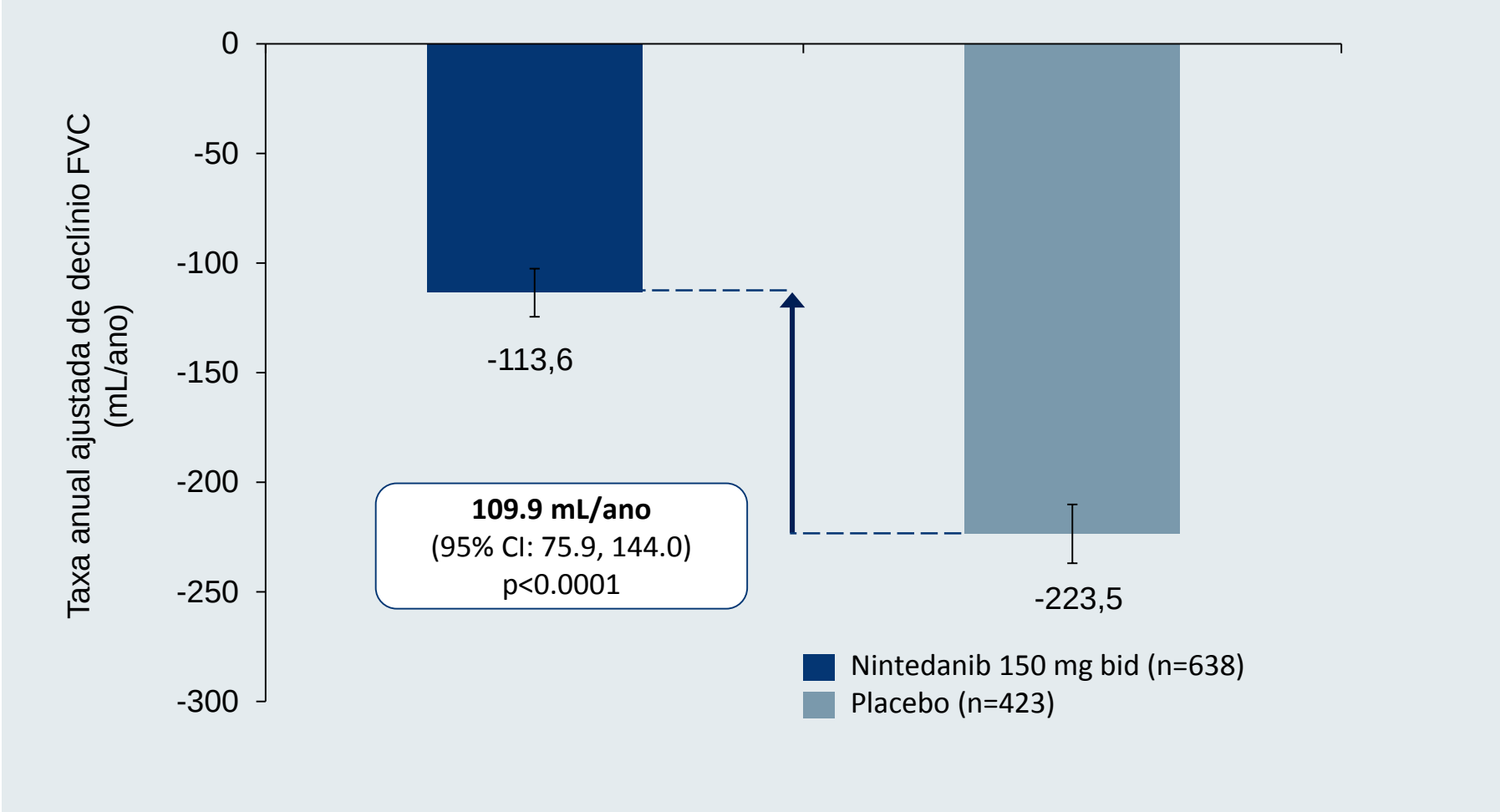
Objetivos secundários

- Tempo até à primeira exacerbação (reportada pelo investigador) durante 52 semanas
- Alteração em relação a *baseline* na pontuação total do St. George's Respiratory Questionnaire (SGRQ) às 52 semanas
- Mortalidade durante 52 semanas

Richeldi L, et al. N Engl J Med 2014;370:2071–2082.

Nintedanib diminuiu a taxa anual de declínio de FVC em 50% vs placebo

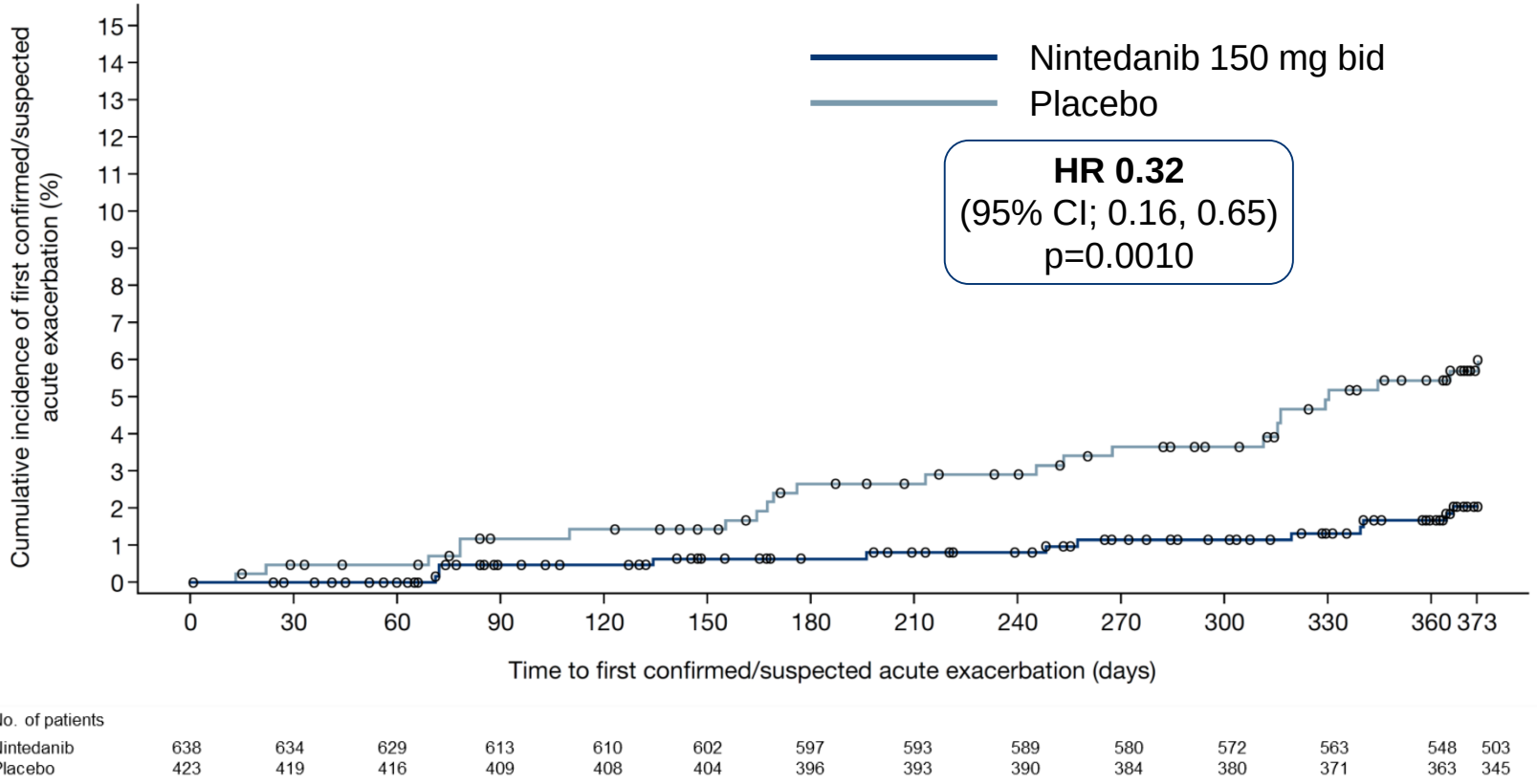
Pooled data



Richeldi L, et al. N Engl J Med 2014;370:2071–2082.

Nintedanib reduziu o risco de exacerbações em 68%

Pooled data

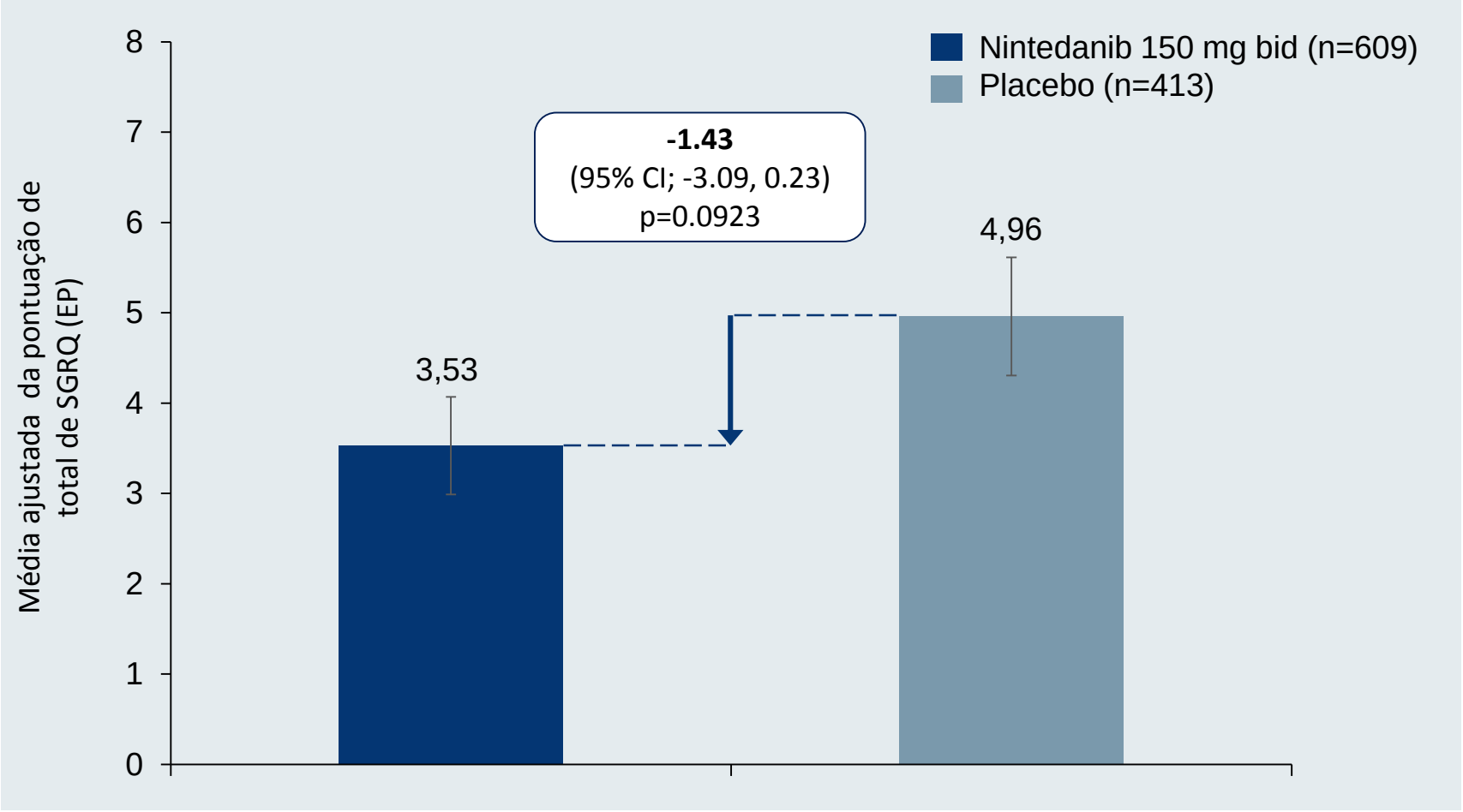


	Nintedanib 150 mg bid (n=638)	Placebo (n=423)
Doentes com ≥1 exacerbação aguda, n (%)	12 (1.9)	24 (5.7)

Richeldi L, et al. N Engl J Med 2014;370:2071–2082.

QoL aferida através do SGRQ

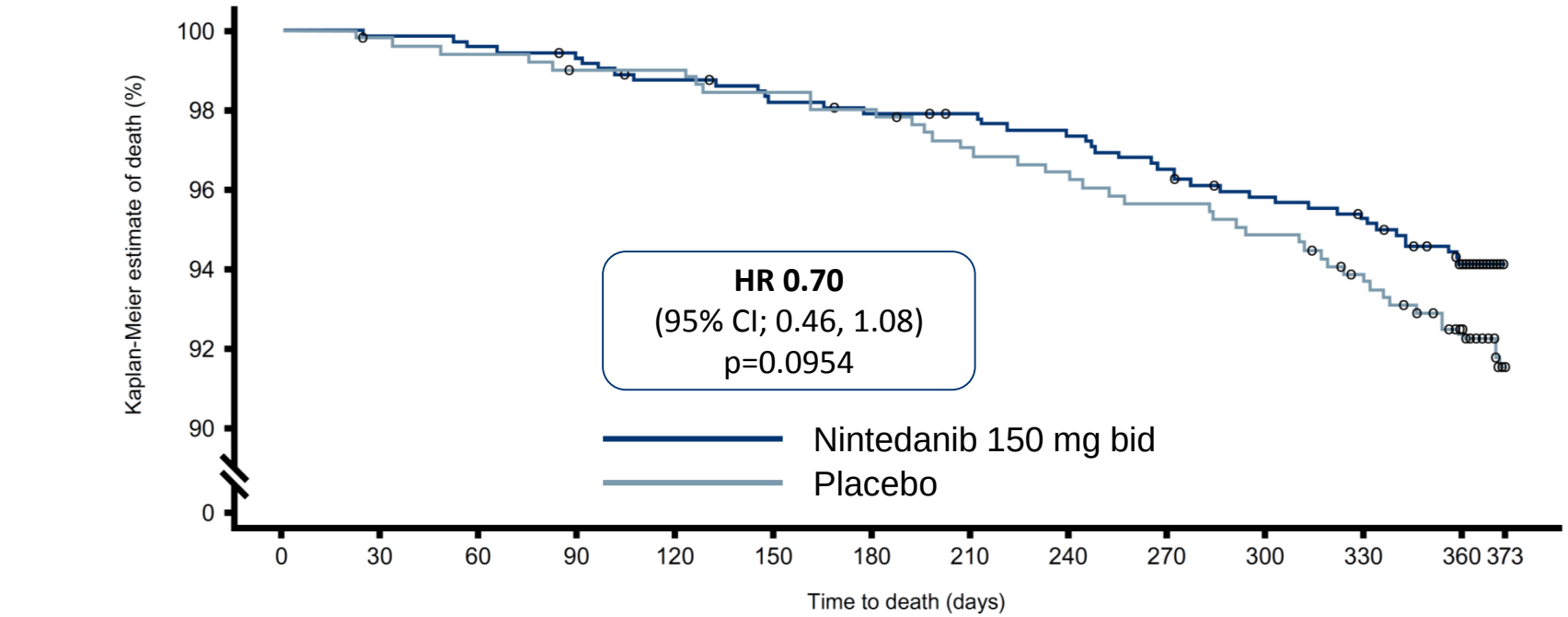
Pooled data



Richeldi L, et al. N Engl J Med 2014;370:2071–2082.

Nintedanib reduziu o risco de mortalidade

Pooled data TOMORROW e INPULSIS®

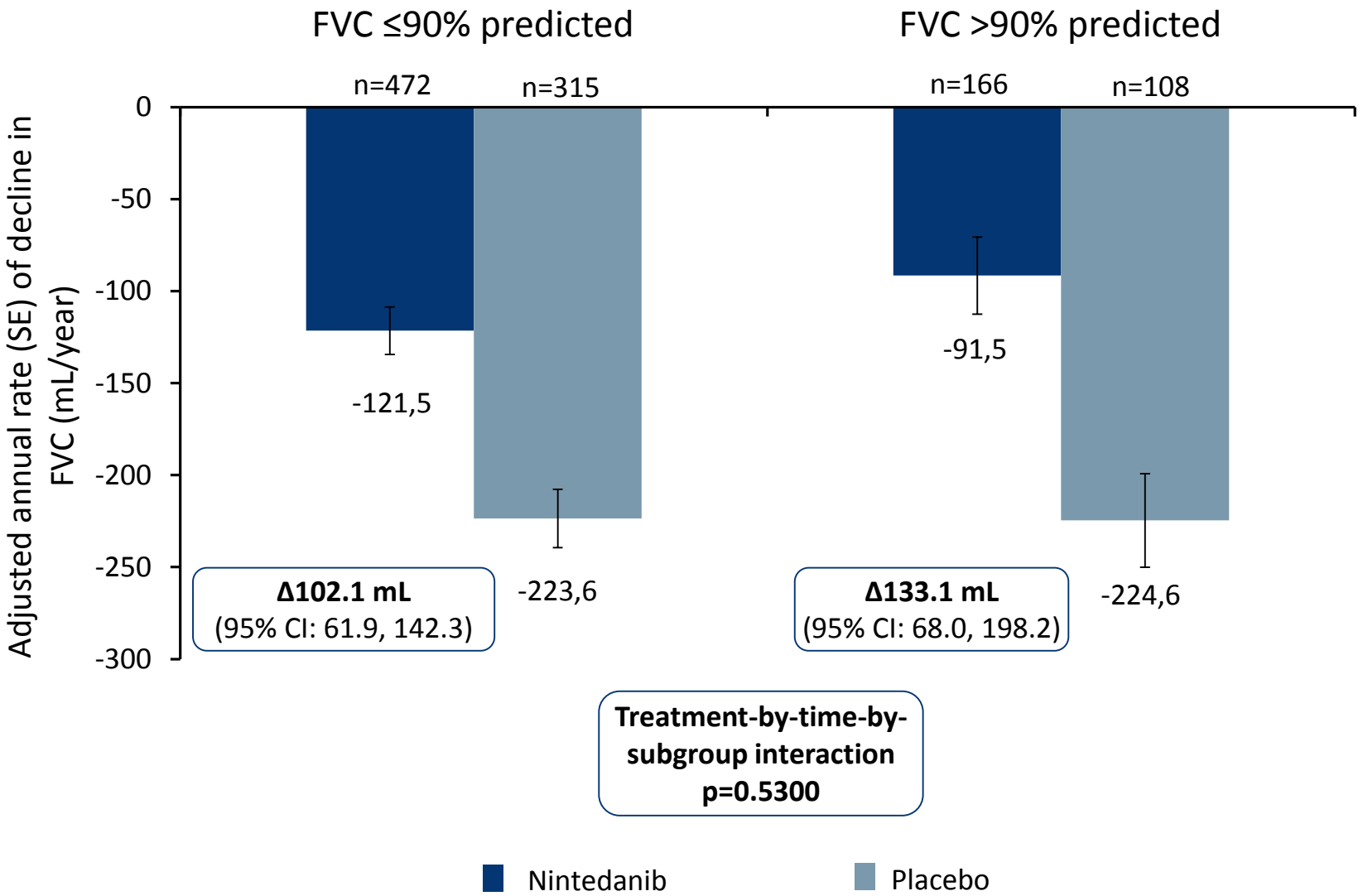


	Nintedanib 150 mg bid (n=723)	Placebo (n=508)
Mortes, n (%)	42 (5.8)	42 (8.3)

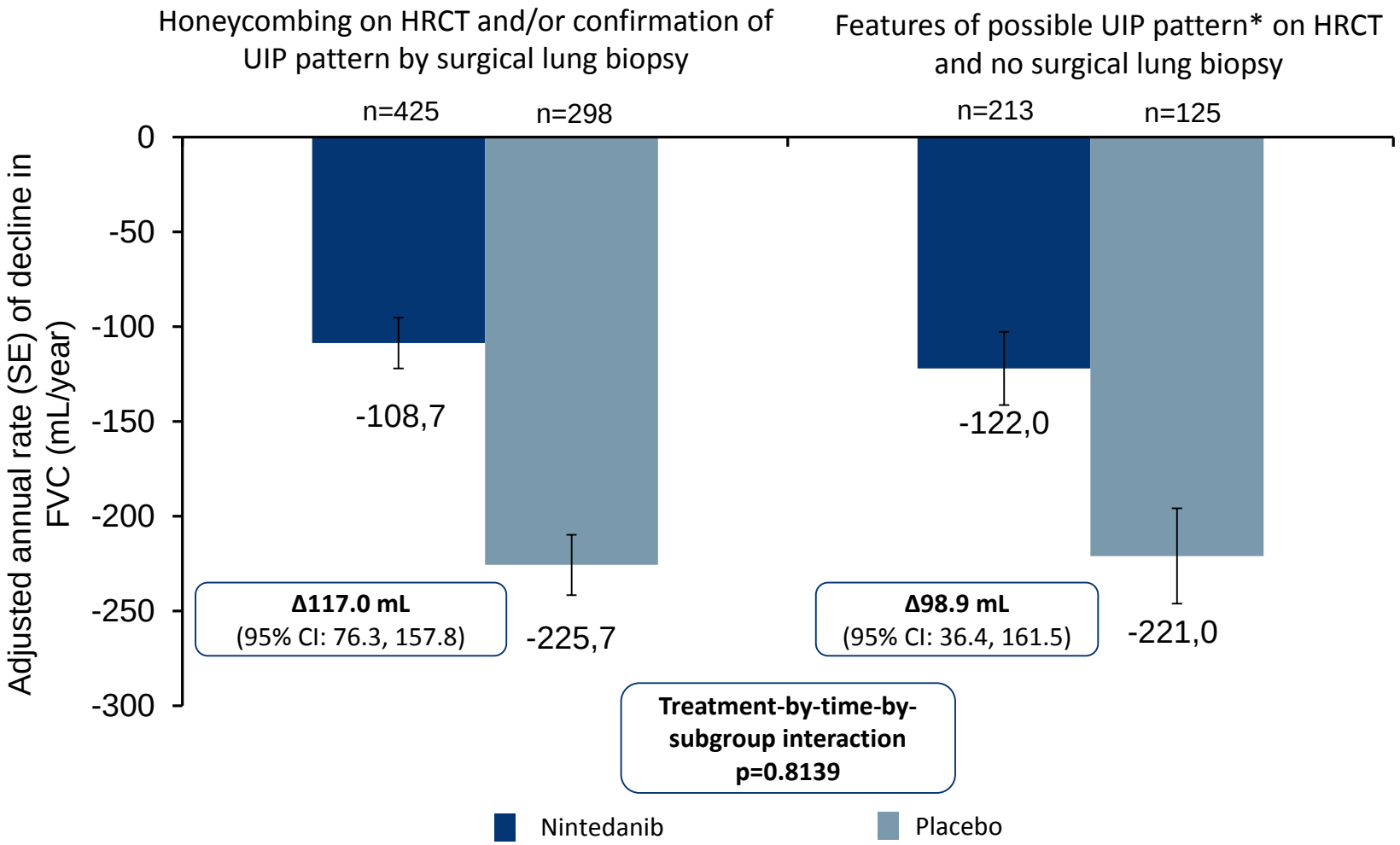
Richeldi L, et al. Presented at International Colloquium on Lung and Airway Fibrosis, Mont Tremblant, Canada, 20–24 September 2014.

Análise de subgrupos

Subgrupo: CVF na *baseline* (≤90%, >90%)

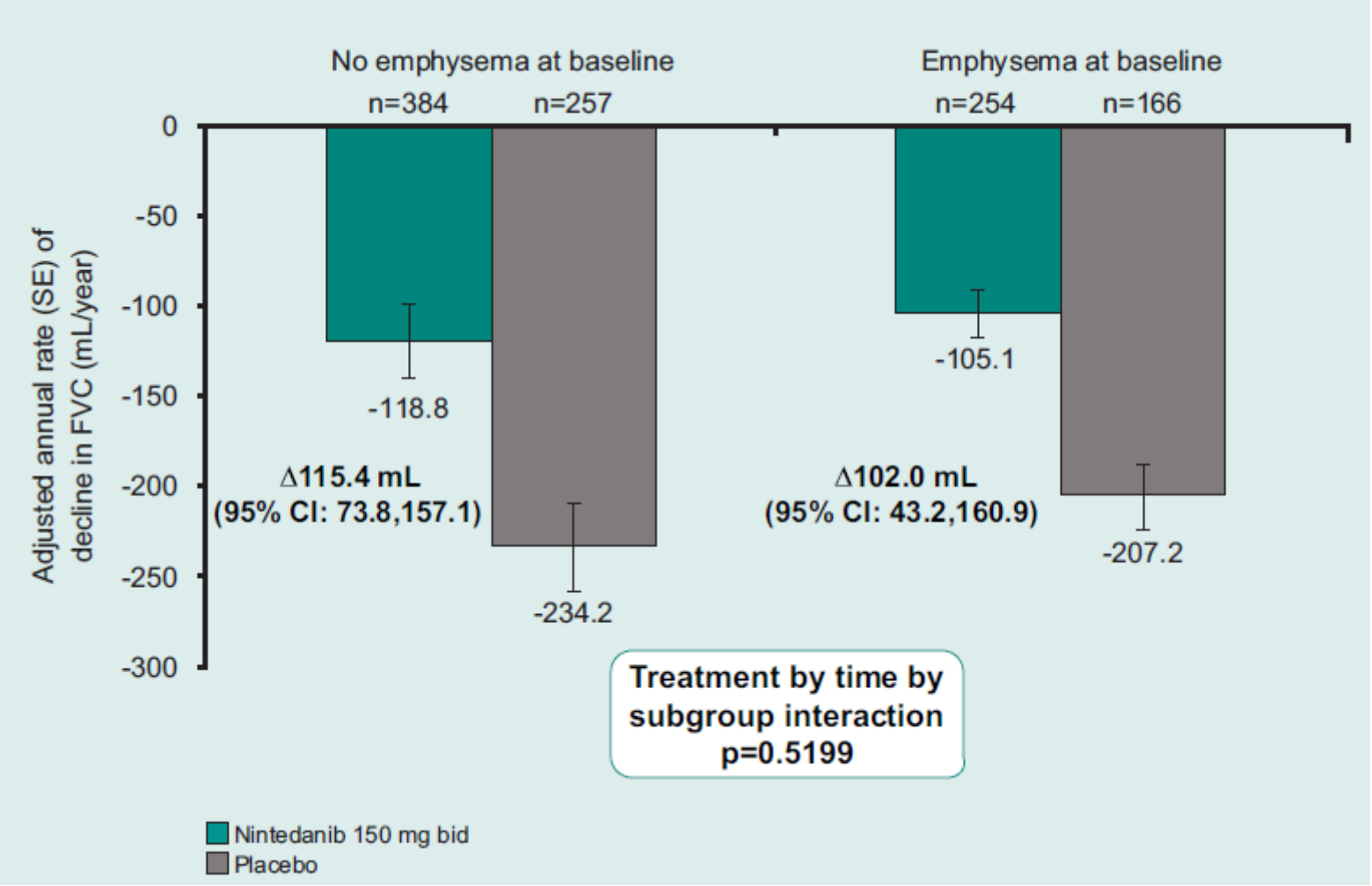


Subgrupo: critérios de diagnóstico da HRCT



*And traction bronchiectasis.

Subgrupo: Presença/ausência de enfisema



Acontecimentos adversos mais frequentes*

Pooled data

N (%)	Nintedanib 150 mg bid (n=638)	Placebo (n=423)
Diarreia	398 (62.4)	78 (18.4)
Náusea	156 (24.5)	28 (6.6)
Diminuição de apetite	68 (10.7)	24 (5.7)
Vómitos	74 (11.6)	11 (2.6)

Acontecimentos adversos com começo após a primeira dose e 28 dias após a última dose

* Acontecimentos adversos reportados em >10% de doentes. †Corresponde ao termo FPI MedDRA, que inclui agravamento da doença e exacerbações de FPI.

Richeldi L, et al. N Engl J Med 2014;370:2071–2082.

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Diminuição de apetite	68 (10.7)	24 (5.7)
Vómitos	74 (11.6)	11 (2.6)

<5% dos pacientes doentes tratados com nintedanib interromperam o tratamento devido a episódios de diarreia

Acontecimentos adversos com começo após a primeira dose e 28 dias após a última dose

* Acontecimentos adversos reportados em >10% de doentes. †Corresponde ao termo FPI MedDRA, que inclui agravamento da doença e exacerbações de FPI.

Richeldi L, et al. N Engl J Med 2014;370:2071–2082.

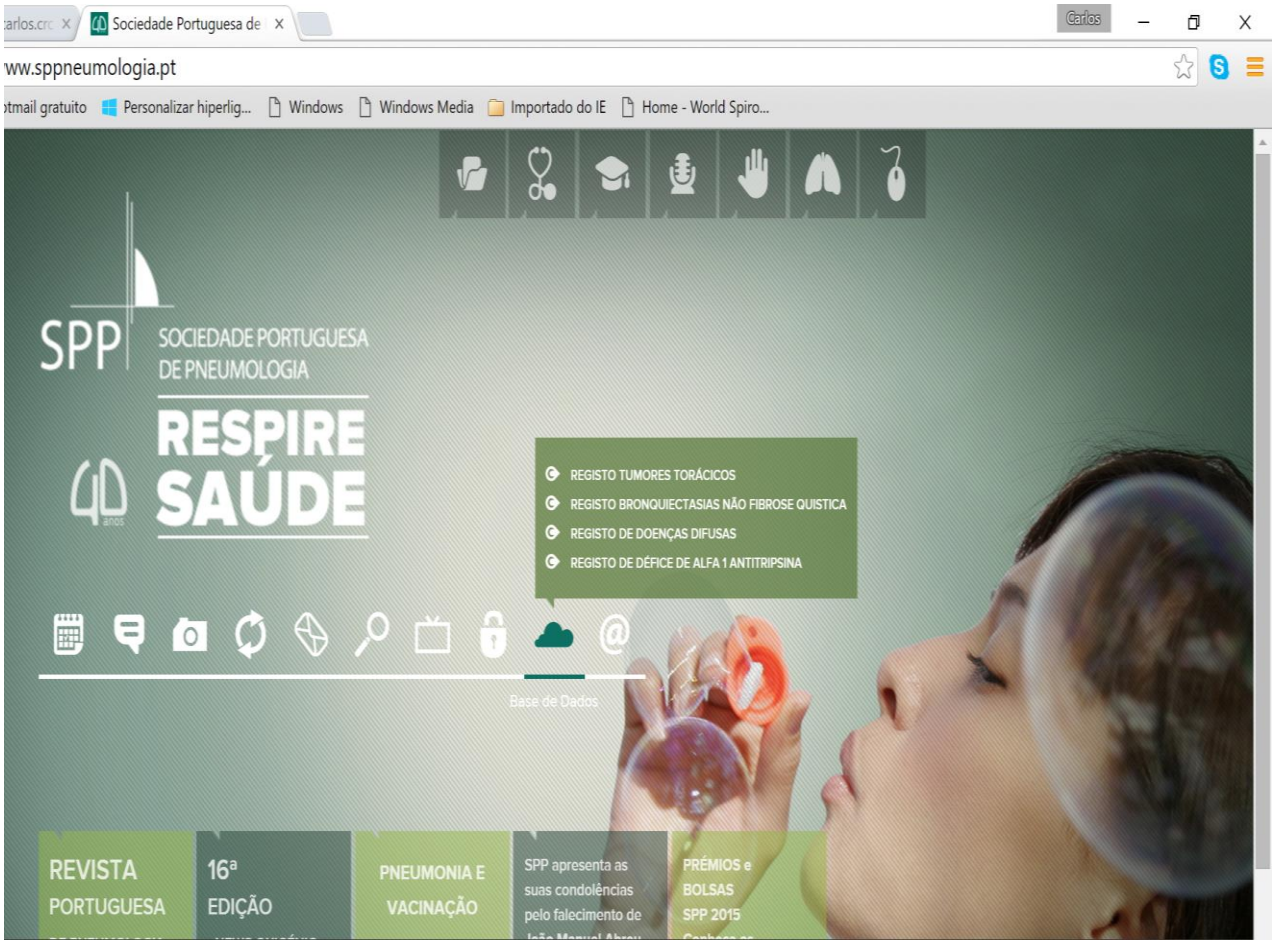
Principais Conclusões

Nintedanib consistentemente atrasa a progressão da IPF através da redução do declínio anual da função pulmonar.

Este efeito clinicamente relevante de nintedanib na progressão da doença foi suportado por:

- Resultados consistentes em vários parâmetros de função pulmonar e análises de sensibilidade
- Redução significativa do risco de exacerbações adjudicadas confirmadas/suspeitas de 68%
- Redução numérica na mortalidade de 30%

Nas análises de sub-grupos nintedanib demonstrou ser consistentemente eficaz nos diferentes subgrupos analisados, observando-se benefícios no atraso da progressão da doença num amplo espectro de doentes.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SAÚDE
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REGISTO BRONQUIECTASIAS NÃO FIBROSE QUISTICA
REGISTO DE DOENÇAS DIFUSAS
REGISTO DE DÉFICE DE ALFA 1 ANTITRIPSINA
Base de Dados
REVISTA
PORTUGUESA
16ª
EDIÇÃO
PNEUMONIA E
VACINAÇÃO
SPP apresenta as
suas condolências
pelo falecimento de
PRÉMIOS e
BOLSAS
SPP 2015

Consensus document for the diagnosis and treatment of idiopathic pulmonary fibrosis

C. Robalo Cordeiro[a,*], P. Campos[b], L. Carvalho[c], S. Campainha[d], S. Clemente[e], L. Figueiredo[f], J.M. Jesus[g], A. Marques[h], C. Souto-Moura[i], R. Pinto Basto[j], A. Ribeiro[k], M. Serrado[j], A. Morais[h]

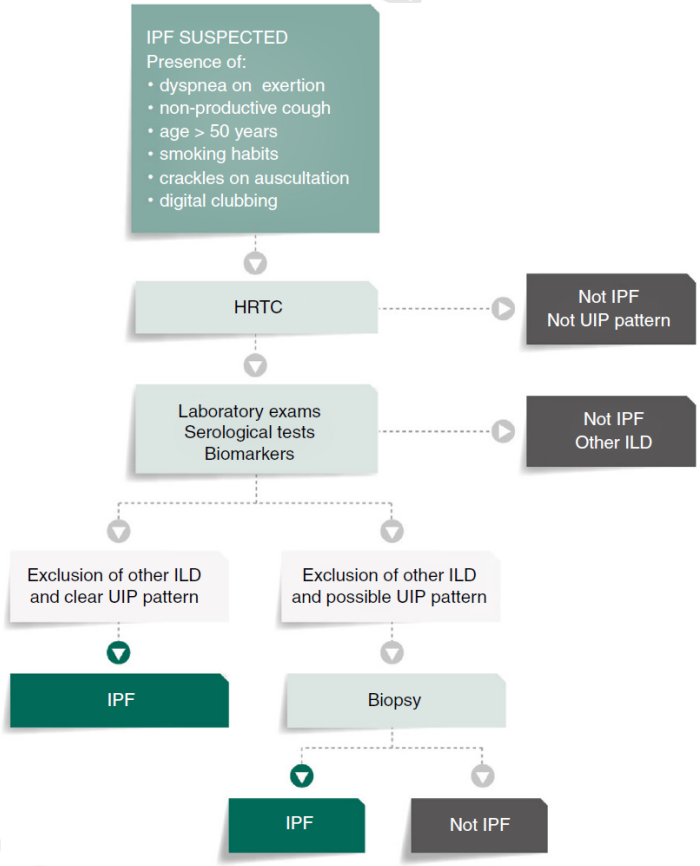

Figure 1 IPF diagnosis algorithm. ILD: interstitial lung disease; IPF: idiopathic pulmonary fibrosis; HRCT: high-resolution computed tomography; UIP: usual interstitial pneumonia.

http://dx.doi.org/10.1016/j.rppnen.2016.01.003

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Table 1 Idiopathic pulmonary fibrosis diagnosis examinations.

At IPF diagnosis
Systematic
Chest HRCT
Plethysmography and DLCO
Arterial blood gas in room air at rest
6MWT with measurement of percutaneous oxygen saturation
Doppler echocardiography
Biology
Antinuclear antibodies
Anti-citrullinated cyclic peptides antibodies
Rheumatoid factor
Extractable Nuclear Antigens antibodies
Occasional
Video-assisted surgical lung biopsy
Differential cell count of BAL
Depending on context
Genetic testing
Anti-neutrophil cytoplasmic antibodies
Creatine phosphokinase
Anti-thyroid antibodies
Precipitins (depending on disease presentation)
Electrophoresis of serum proteins, immuno-electrophoresis of serum proteins, urine immunofixation and cryoglobulinaemia
Exploration for gastro-oesophageal reflux
Exploration for sleep apnoea syndrome

Adapted from Cottin et al.[3]
6MWT: 6-min walk test; BAL: bronchoalveolar lavage; DLCO: diffusing capacity of the lung for carbon monoxide; HRCT: high-resolution computed tomography.

http://dx.doi.org/10.1016/j.rppnen.2016.01.003

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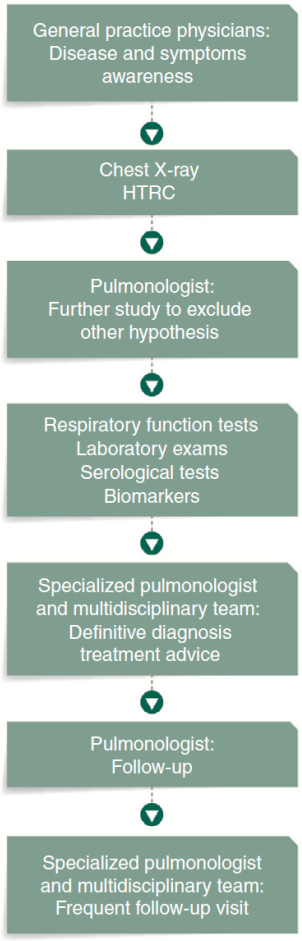

Figure 3 Idiopathic pulmonary fibrosis patient flow. HRCT: high-resolution computed tomography.

http://dx.doi.org/10.1016/j.rppnen.2016.01.003

Consensus document for the diagnosis and treatment of idiopathic pulmonary fibrosis

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Table 4 Idiopathic pulmonary fibrosis management examinations.

During IPF follow-up
Every 6 months
FVC and DLCO
Arterial blood gas in room air
6MWT
Chest X ray
Depending on context
Chest HRCT
Doppler echocardiography
TLC
Right heart catheterization

Adapted from Cottin et al.[3]
6MWT: 6-min walk test; DLCO: diffusing capacity of the lung for carbon monoxide; FVC: forced vital capacity; HRCT: high-resolution computed tomography; TLC: total lung capacity.

http://dx.doi.org/10.1016/j.rppnen.2016.01.003

CENTROS DE ALTA DIFERENCIAÇÃO EM PATOLOGIA INTERSTICIAL

CENTROS DE ALTA DIFERENCIAÇÃO EM PATOLOGIA INTERSTICIAL

- 1 por 1.500.000 habitantes no Reino Unido (1 por 3.000.000 em Portugal?)
- Recursos: Broncologia, Cirurgia Torácica, Consultores especialistas (pneumologia, radiologia, patologia)

CENTROS SATÉLITES

- 4 a 6 centros satélites por cada centro de alta diferenciação

INDICADORES DE MONITORIZAÇÃO DA REDE

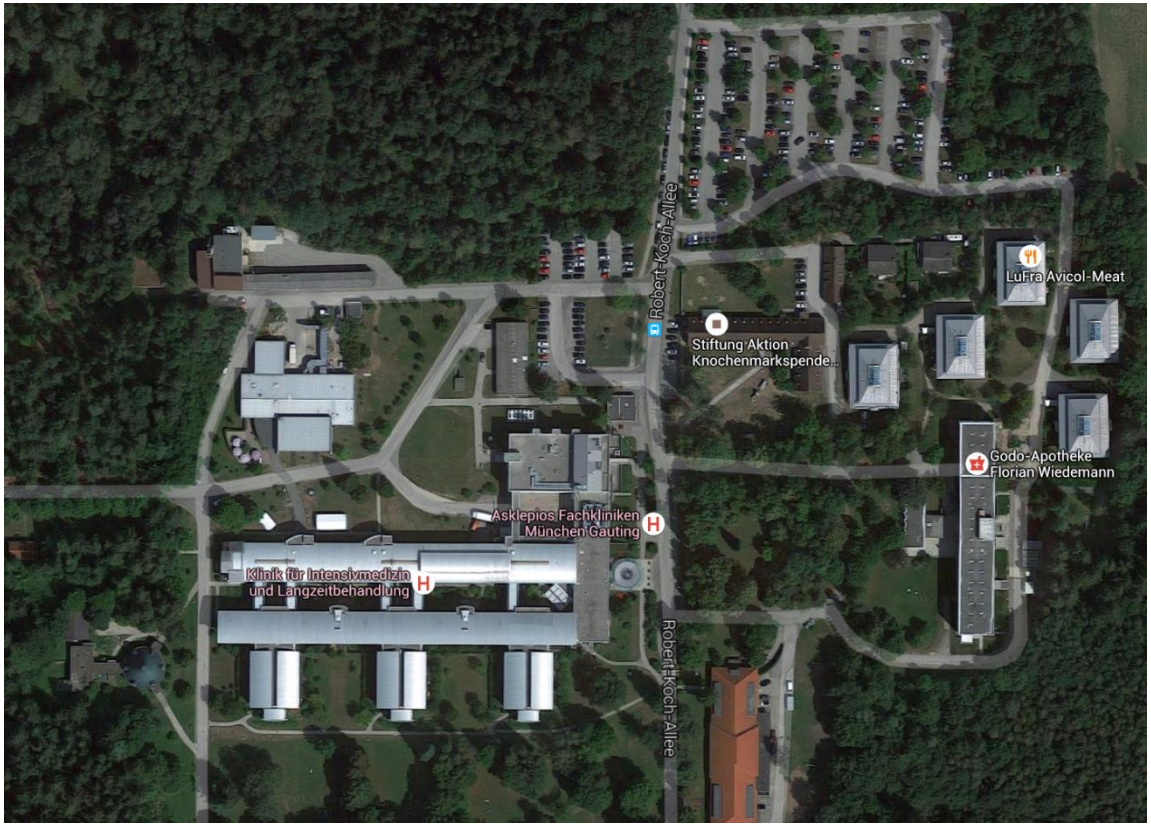
- Periodicidade de Reuniões
- Casos/Reunião
- Diagnósticos clínicos/cirúrgicos

CENTROS DE ALTA DIFERENCIAÇÃO EM PATOLOGIA INTERSTICIAL

Composição mínima da Equipa Multidisciplinar envolvida no diagnóstico de patologia intersticial/Fibrose Pulmonar Idiopática

Etapas do diagnóstico	**Composição da Equipa Multidisciplinar (todos os profissionais de saúde devem ser peritos em patologia intersticial)**
Na avaliação clínica, do estudo funcional e da TAC	Pneumologista consultor Radiologista consultor Coordenador da Equipa Multidisciplinar
Na decisão de realização de Lavado Broncoalveolar (LBA) e/ou Biópsia Pulmonar Transbrônquica (BPTB) ou Biópsia Pulmonar Cirúrgica (BPC) Apenas alguns doentes	Pneumologista consultor Radiologista consultor Patologista consultor Cirurgião Torácico quando necessário Coordenador da Equipa Multidisciplinar
Na avaliação dos resultados do LBA, BPTB ou BPC	Pneumologista consultor Radiologista consultor Patologista consultor Coordenador da Equipa Multidisciplinar

CPC Comprehensive Pneumology Center



Clínica respiratória Asklepius

Clínica especializada em Pneumologia

268 camas

20.000 novos doentes/ano

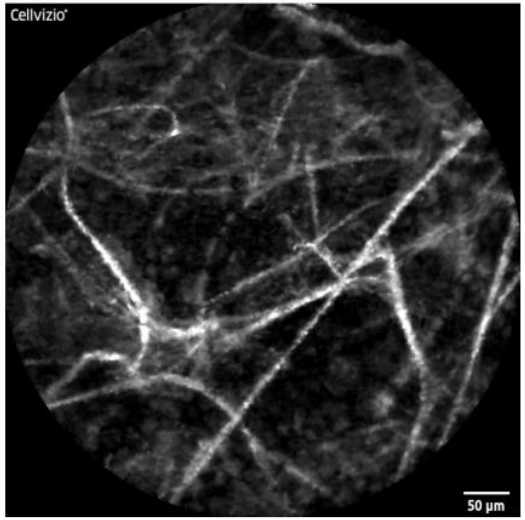
- **400 com ILD**

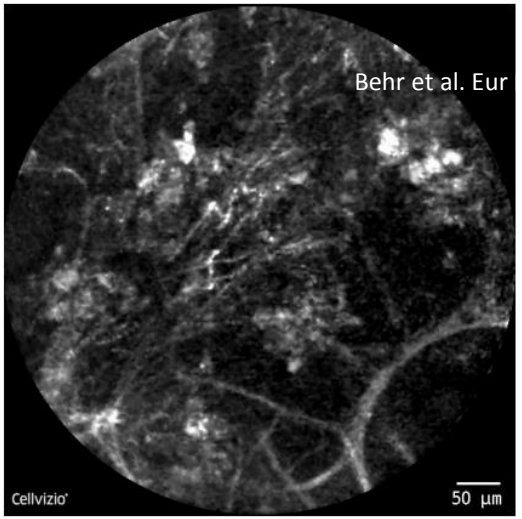
Pneumologistas, CCT, Cardiologia, Anestesistas, Patologista, Radiologista

PFR, Broncoscopia e CCT

Management of patients with idiopathic pulmonary fibrosis in clinical practice: the INSIGHTS-IPF registry

Jürgen Behr[1], Michael Kreuter[1], Marius M. Hoeper[1], Hubert Wirtz[1], Jens Klotsche[1], Dirk Koschel, Stefan Andreas, Martin Claussen, Christian Grohé, Henrike Wilkens, Winfried Randerath, Dirk Skowasch, F. Joachim Meyer, Joachim Kirschner, Sven Gläser, Felix J.F. Herth, Tobias Welte, Rudolf Maria Huber, Claus Neurohr, Martin Schwaiblmair, Martin Kohlhäufl, Gert Höffken, Matthias Held, Andrea Koch, Thomas Bahmer and David Pittrow[1]





SMILLING BAL CELL