Fibrose Pulmonaire Idiopathique
Actualités thérapeutiques

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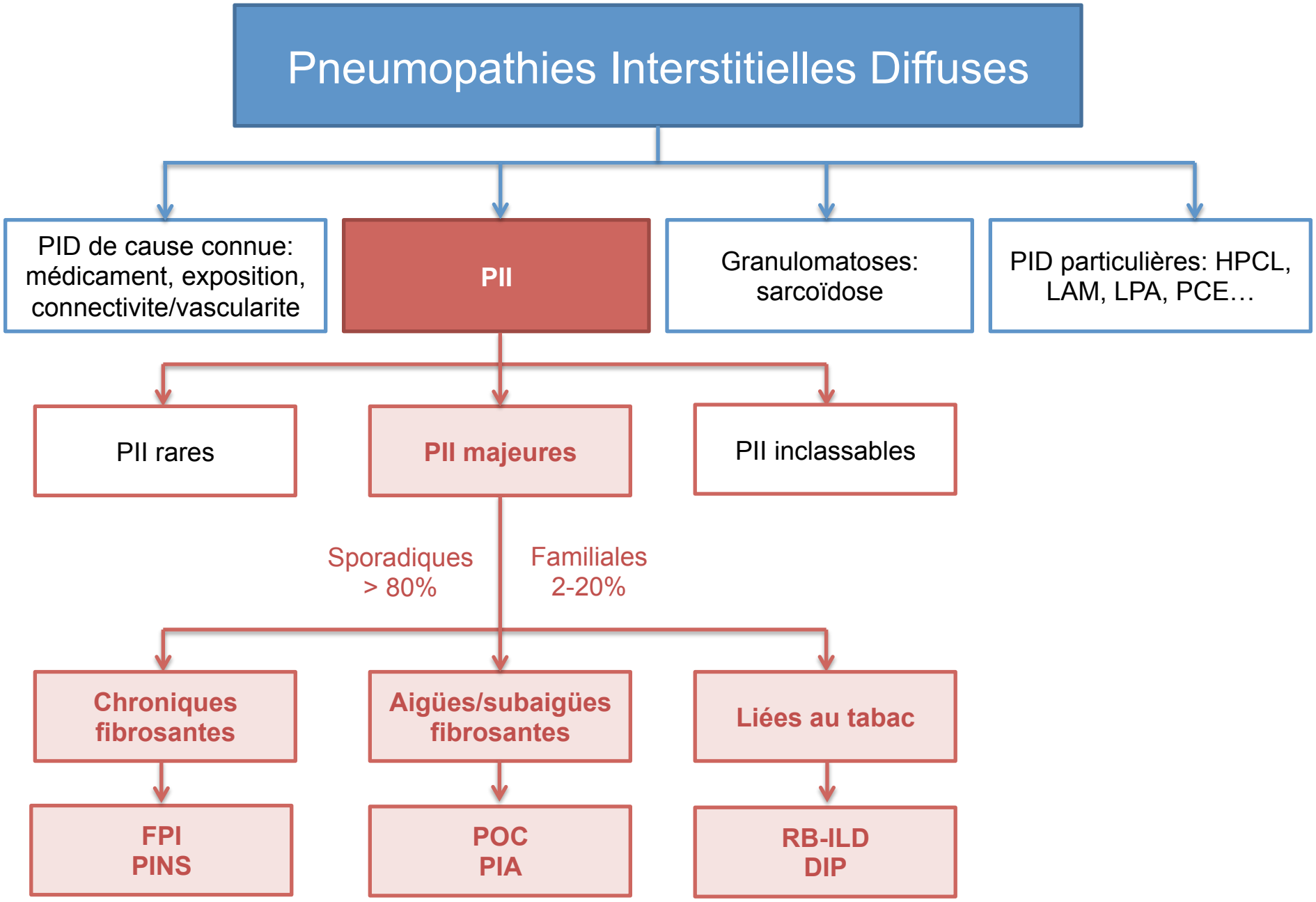
UNIVERSITÉ PARIS 13 NORD

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS



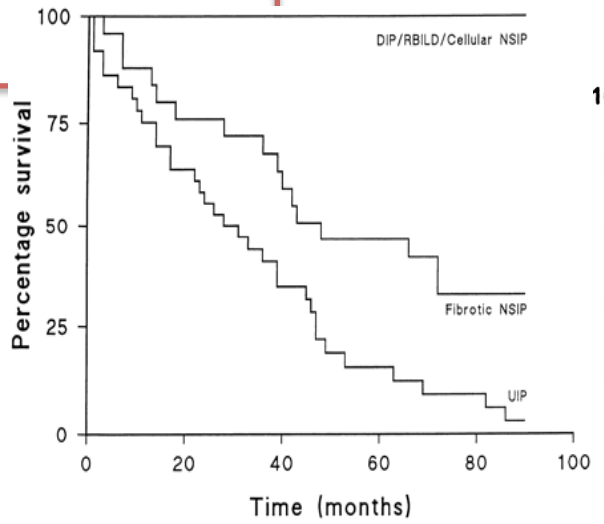
ATS/ERS statement update. *AJRCCM* 2013

Pneumopathies Interstitielles Diffuses

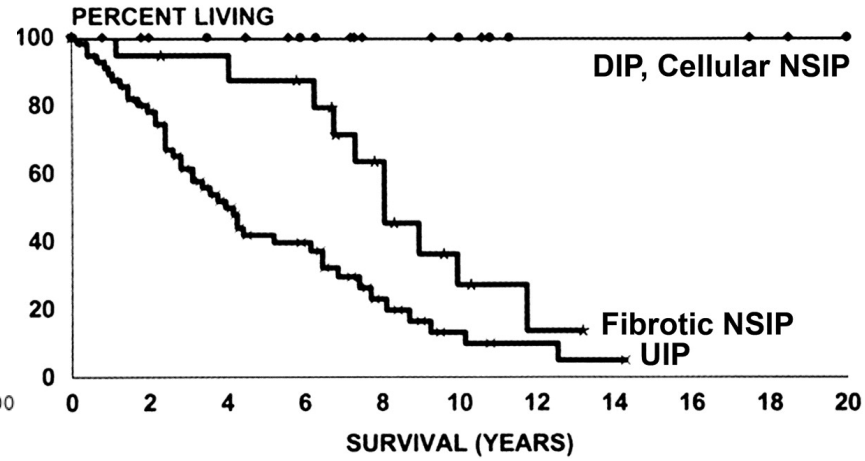
- PID de cause connue: médicament, exposition, connectivite/vascularite
- **PII**
- Granulomatoses: sarcoïdose
- PID particulières: HPCL, LAM, LPA, PCE

PII

- PII rares
- **PII majeures**
  - **Chroniques fibrosantes**
    - **FPI**
    - **PINS**
- PII inclassables



Nicholson et al. *AJRCCM* 2000

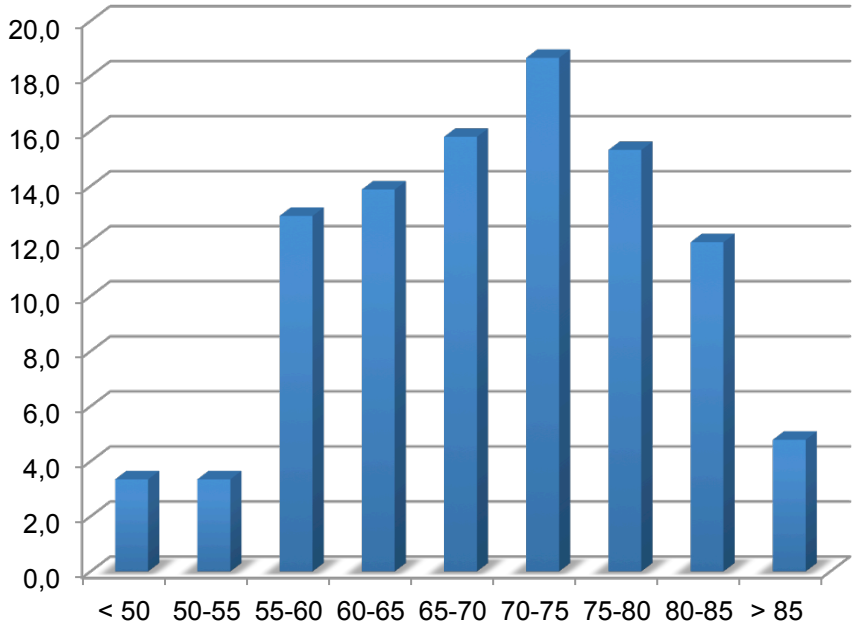


Travis et al. *Am J Surg Pathol 2000*

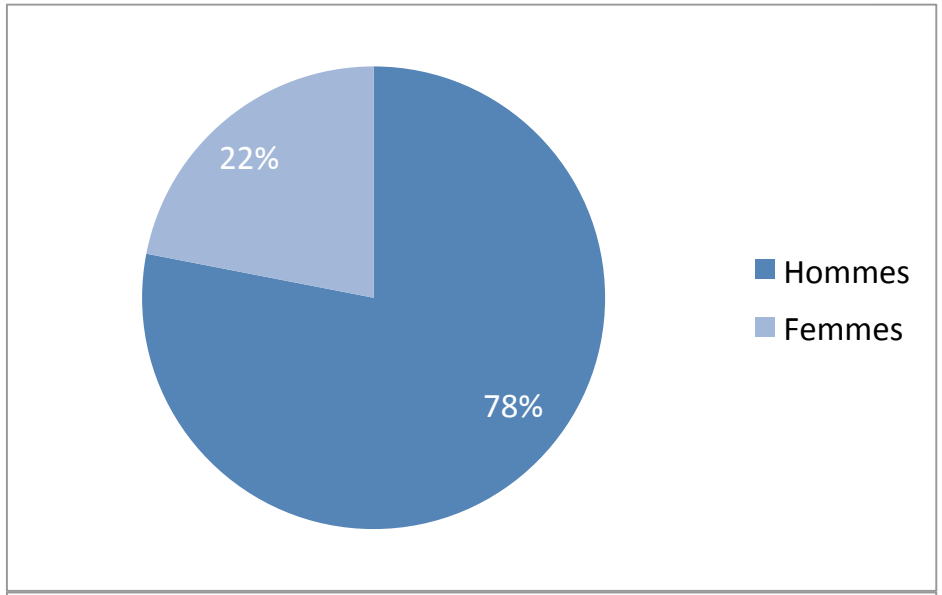
Epidemiologie

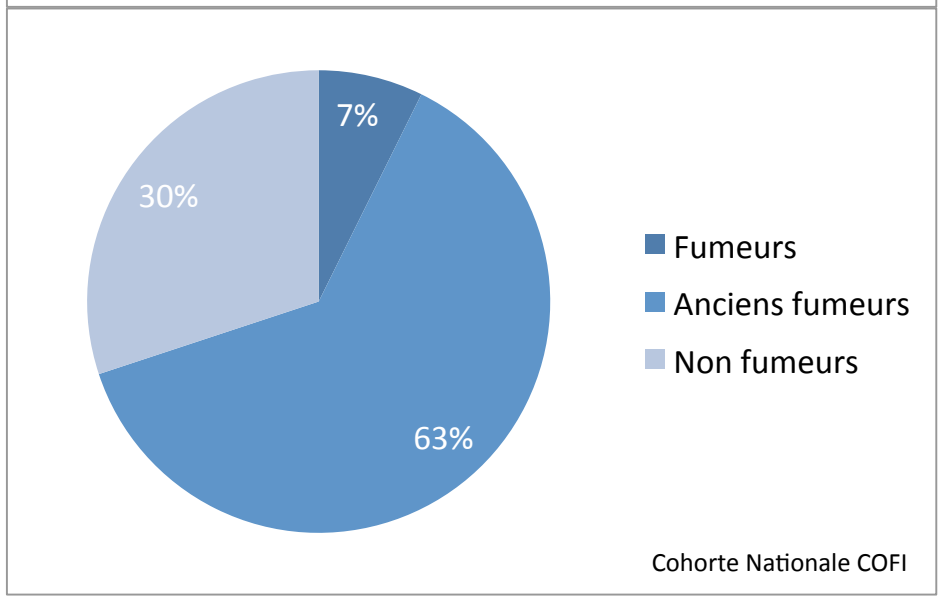
- Prévalence: 3.4-20.2/100000
- Incidence: 0.93-10.7/100000/an
- Les 3 plus fréquentes PID > 50% des cas : sarcoïdose, FPI et connectivites

Coultas et al. *AJRCCM* 1994
Karakatsani et al. *Respir Med* 2009



Age moyen: 68.8 ± 10.5 ans (29-90)



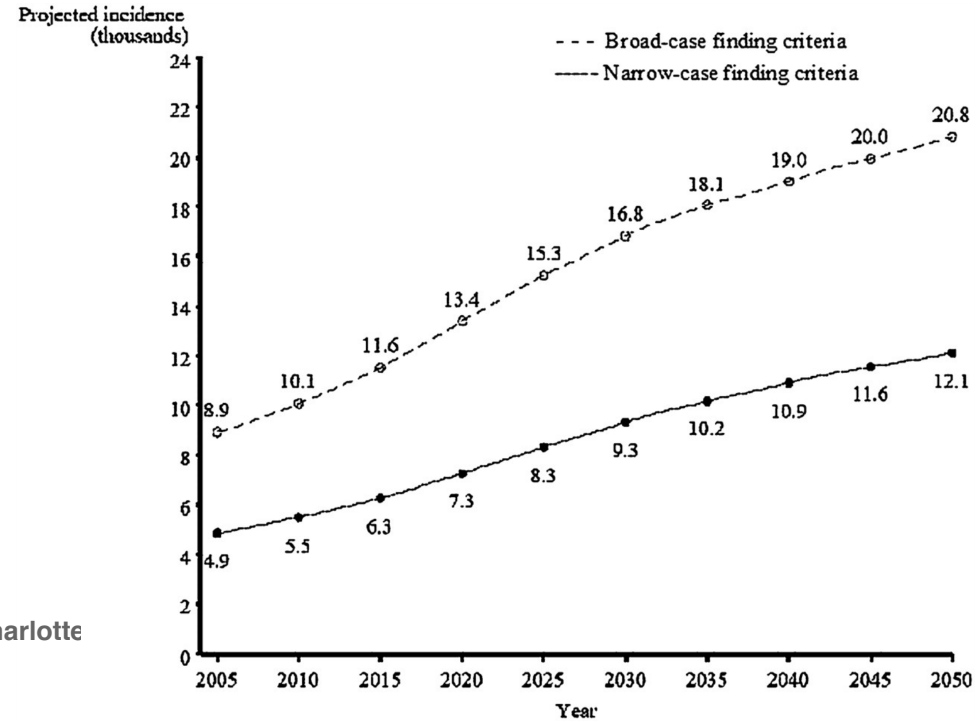


Cohorte Nationale COFI

Incidence, Prevalence, and Clinical Course of Idiopathic Pulmonary Fibrosis: A Population-Based Study

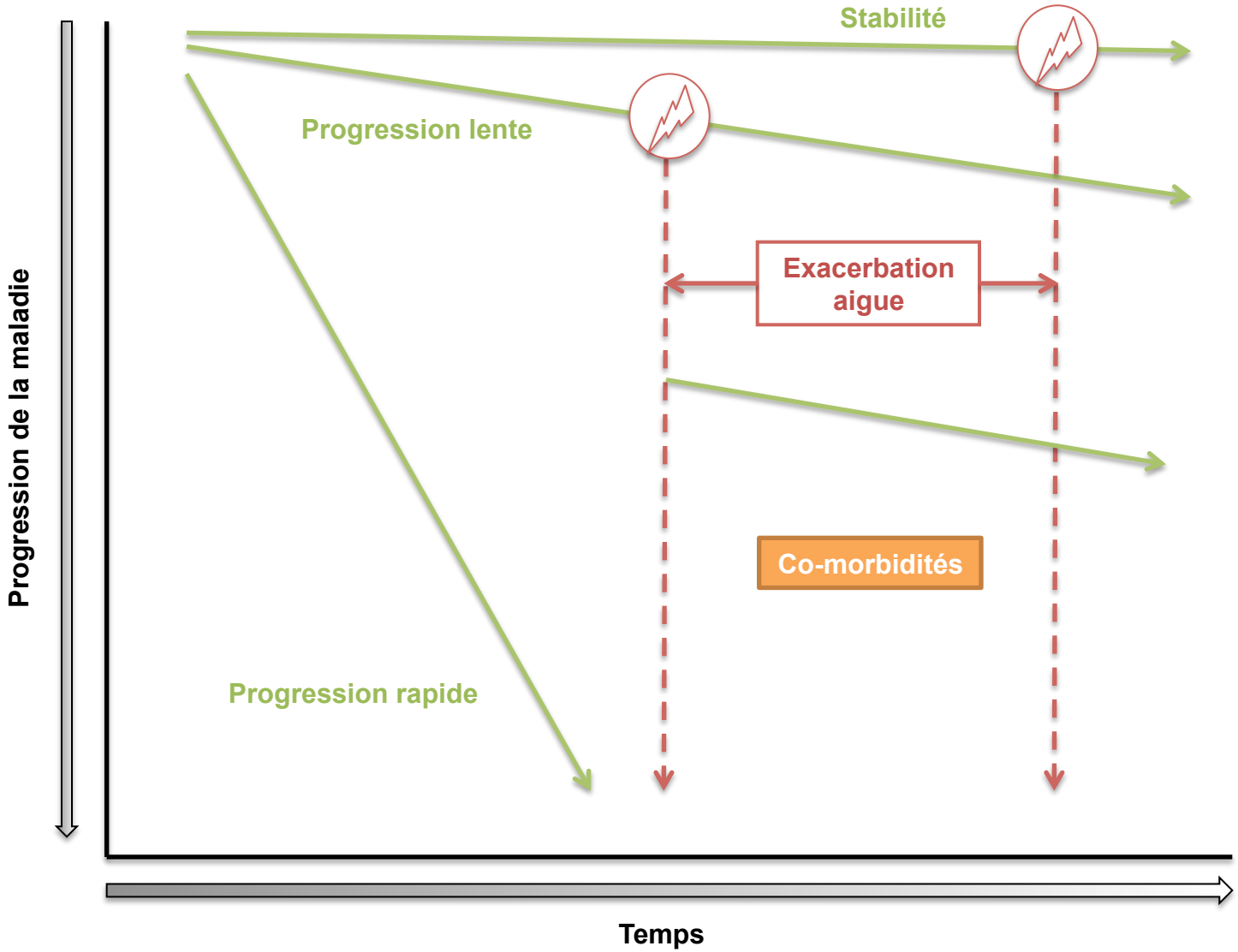
Fernandez-Perez et al. *Chest* 2010

CHEST

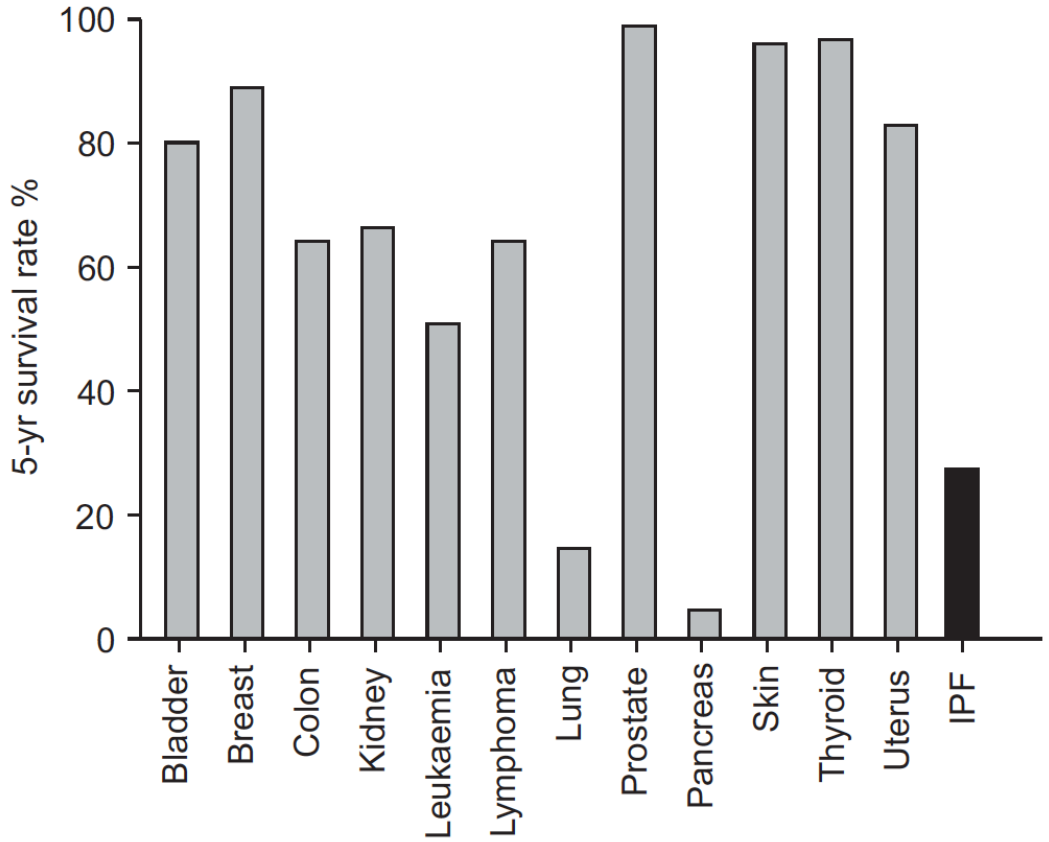


Projected number of individuals with IPF in the United States between 2005 and 2050, assuming no further increase in age-adjusted IPF incidence rate, as evident in 2003 to 2005

Histoire naturelle



Mortalité



Mediane de survie = 2.5-3.5 ans après le diagnostic

Vancheri C et al. *Eur Respir J* 2010

- Augmentation des déclarations de DC liés à la FPI dans la population générale (EU et UK)
- 5000 décès /an (UK)

Olson et al. *Am J Respir Crit Care Med* 2006
Navaratnam et al. *Thorax* 2011

Diagnostic de FPI: ATS/ERS/JRS/ALAT 2011

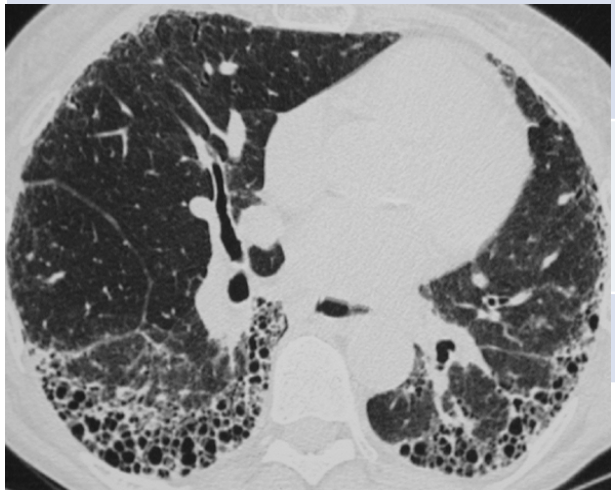
- Exclusion des autres causes de PID: toxicité médicamenteuse, exposition environnementale/professionnelle et connectivite/vascularite
- Aspect de PIC sur la TDM chez les patients non soumis à une BPC
- Combinaisons spécifiques de la probabilité diagnostique de la TDM et de de la probabilité diagnostique de l'histologie en cas de BPC

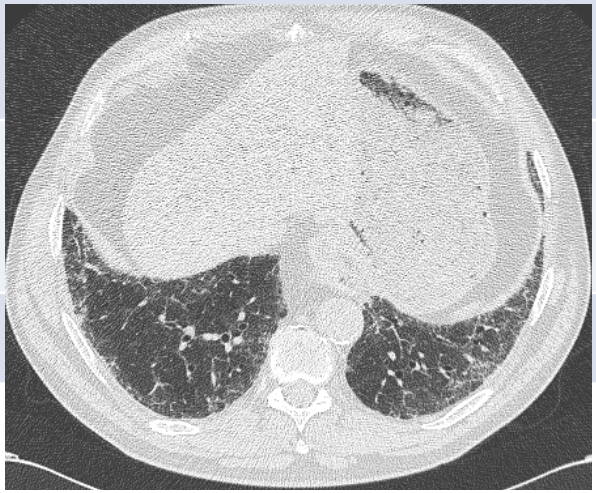
- LBA ou BTB non nécessaire systématiquement, mais laissés à l'appréciation du clinicien
- Discussion multidisciplinaire entre experts pneumologues, radiologues et anatomo-pathologistes

ATS/ERS/JRS/ALAT 2011. *Am J Respir Crit Care Med* 2011
Recommandations pratiques pour le diagnostic et la prise en charge de la FPI. *Rev Mal Respir* 2013

Critères TDM de PIC

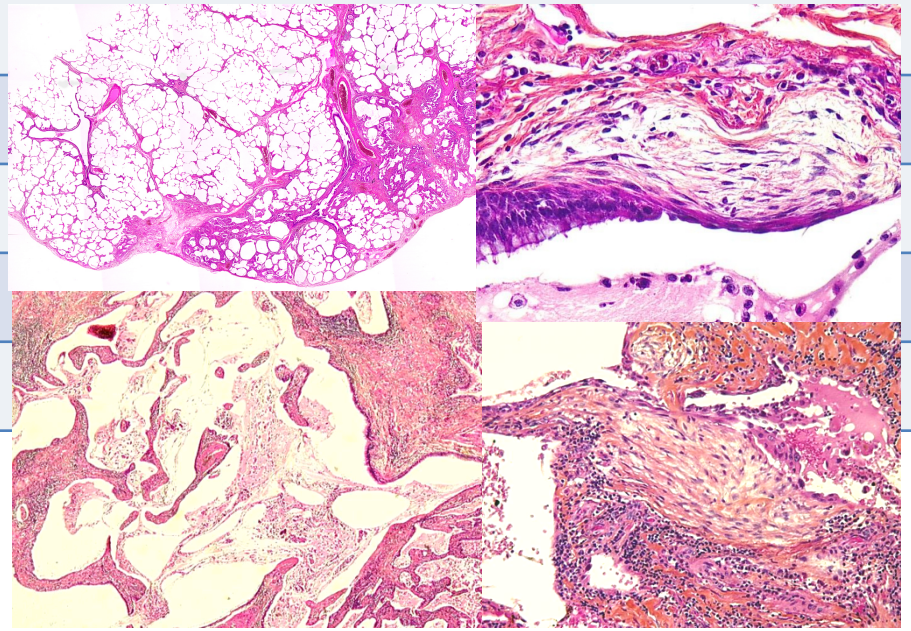
Pattern de PIC (tous les 4 signes)	Pattern de PIC possible (tous les 3 signes)	Incompatible avec un pattern de PIC (un des 7 signes)
Prédominance sous-pleurale, et basale	Prédominance sous-pleurale, et basale	Prédominance supérieure ou moyenne
Réticulations	Réticulations	Prédominance PBV
Rayon de miel avec ou sans bronchiectasies par traction	Absence de signes incompatibles avec un pattern de PIC	VD extensif (> réticulations)
Absence de signes incompatibles avec un pattern de PIC		Micronodules diffus (bilateraux, prédominant aux lobes sup)
		Kystes isolés (multiples, bilateraux, à distance du RM)
		Perfusion en mosaïque diffuse/ air trapping (bilateral, dans > 3 lobes)
		Consolidations

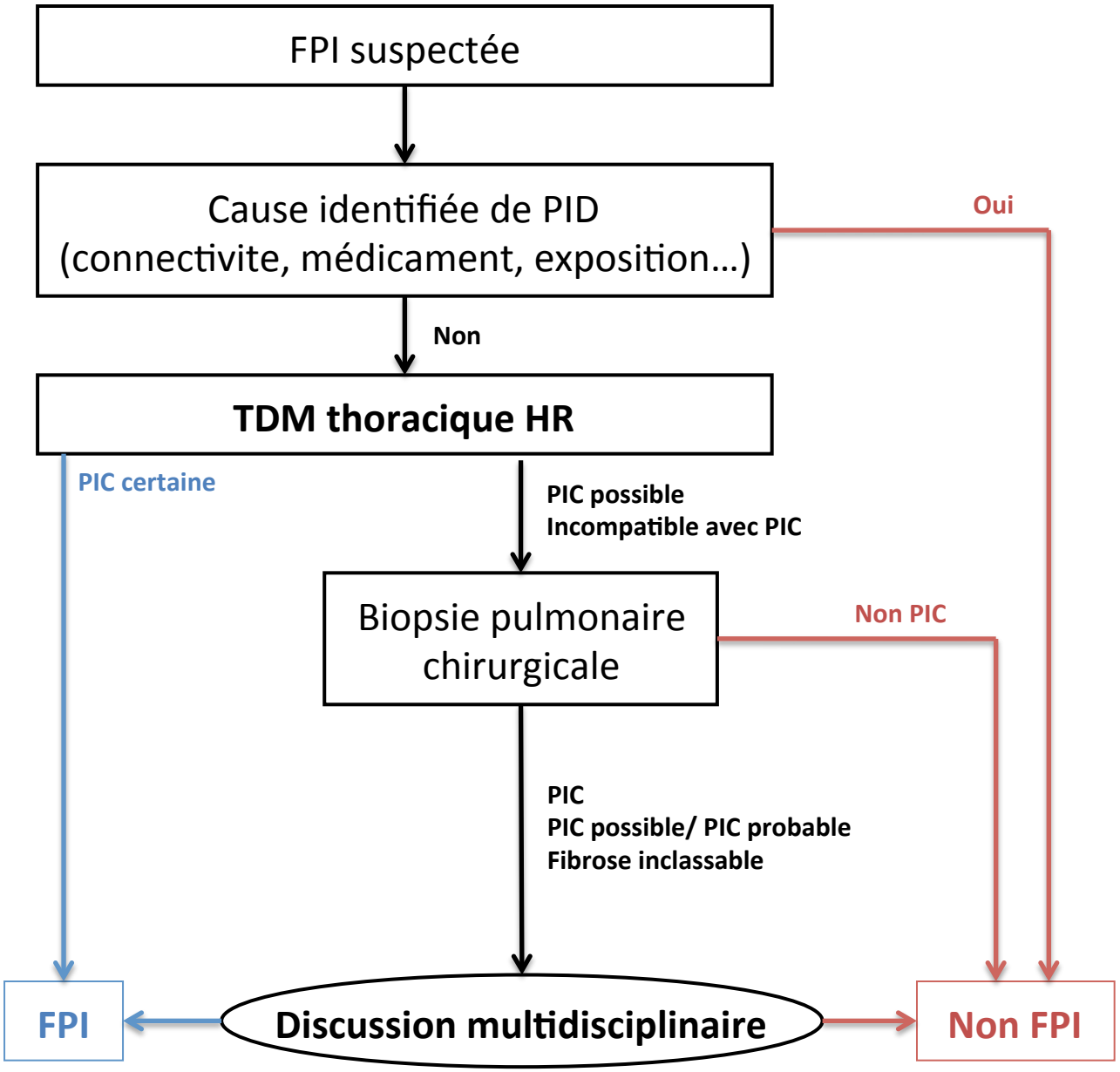




Critères histologiques de PIC

Pattern de PIC (tous les 4 critères)	• Fibrose marquée/distorsion architecturale ± rayon de miel avec une distribution à prédominance sous-pleurale/ paraseptale • Atteinte « patchy » (hétérogénéité temporelle et spatiale) • Présence de foyers fibroblastiques • Absence de signes contre le diagnostic de PIC suggérant un diagnostic alternatif
Pattern de PIC probable	
Pattern de PIC possible	
Pas pattern de PIC	
Fibrose inclassable	

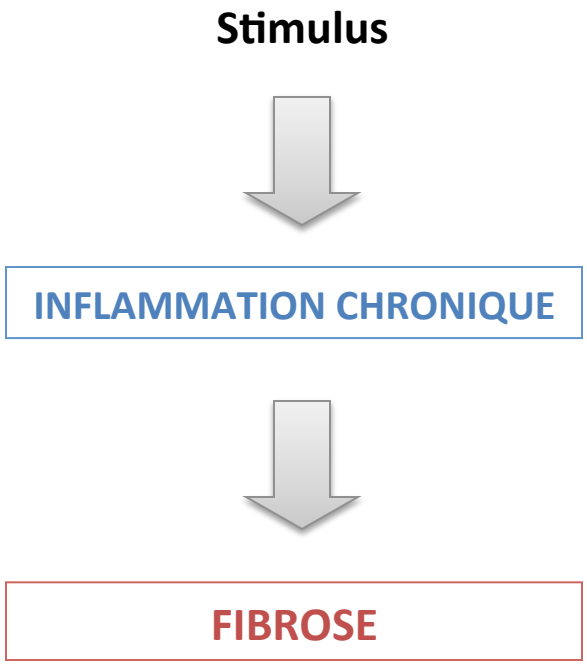



FPI suspectée
Cause identifiée de PID
(connectivite, médicament, exposition…)
Oui
Non
TDM thoracique HR
PIC certaine
PIC possible
Incompatible avec PIC
Biopsie pulmonaire
chirurgicale
Non PIC
PIC
PIC possible/ PIC probable
Fibrose inclassable
FPI
Discussion multidisciplinaire
Non FPI

Diagnostic de FPI: DMD

Pattern HRCT	Biopsie pulmonaire chirurgicale (si réalisée)	Diagnostic de FPI ?
PIC	PIC	OUI
	Probable PIC	
	Possible PIC	
	Fibrose non classable	
	Pas PIC	Non
Possible PIC	PIC	OUI
	Probable PIC	
	Possible PIC	Probable
	Fibrose non classable	Non
	Pas PIC	
Incompatible avec PIC	PIC	Possible
	Probable PIC	
	Possible PIC	Non
	Fibrose non classable	
	Pas PIC	

Hypothèse pathogénique historique



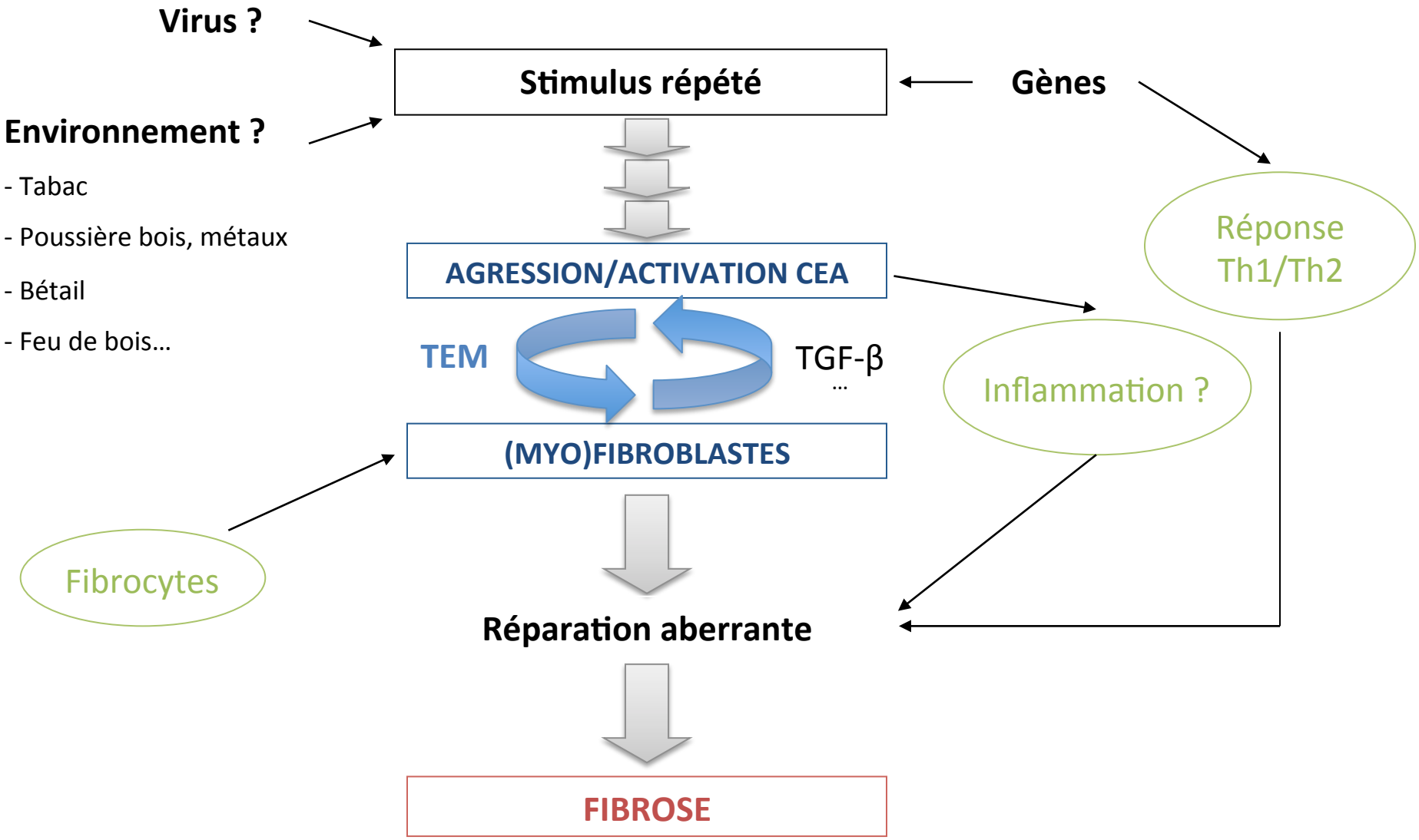
Idiopathic Pulmonary Fibrosis: Diagnosis and Treatment

International Consensus Statement

This Joint Statement of the American Thoracic Society (ATS), and the European Respiratory Society (ERS) was Adopted by the ATS Board of Directors, July 1999 and by the ERS Executive Committee, October 1999

- **Recommandations non fondées sur des preuves**
- Association :
  - Prednisone: 0.5 mg/kg/j pendant 4 semaines, 0.25 mg/kg/j pendant 8 semaines, puis 0.125 mg/kg/j ou 0.25mg/kg/2j
  - Et Azathioprine : 2-3 mg/kg/j (<150 mg/j) ou Cyclophosphamide: 2 mg/kg/j
  - Pendant au moins 6 mois en l'absence de complications

Hypothèse pathogénique récente



An Official ATS/ERS/JRS/ALAT Statement: Idiopathic Pulmonary Fibrosis: Evidence-based Guidelines for Diagnosis and Management

Ganesh Raghu, Harold R. Collard, Jim J. Egan, Fernando J. Martinez, Juergen Behr, Kevin K. Brown, Thomas V. Colby, Jean-François Cordier, Kevin R. Flaherty, Joseph A. Lasky, David A. Lynch, Jay H. Ryu, Jeffrey J. Swigris, Athol U. Wells, Julio Ancochea, Demosthenes Bouros, Carlos Carvalho, Ulrich Costabel, Masahito Ebina, David M. Hansell, Takeshi Johkoh, Dong Soon Kim, Talmadge E. King, Jr., Yasuhiro Kondoh, Jeffrey Myers, Nestor L. Müller, Andrew G. Nicholson, Luca Richeldi, Moisés Selman, Rosalind F. Dudden, Barbara S. Griss, Shandra L. Protzko, and Holger J. Schünemann, on behalf of the ATS/ERS/JRS/ALAT Committee on Idiopathic Pulmonary Fibrosis

This Official Statement of the American Thoracic Society (ATS), the European Respiratory Society (ERS), the Japanese Respiratory Society (JRS), and the Latin American Thoracic Association (ALAT) Was Approved by the ATS Board of Directors, November 2010, the ERS Executive Committee, September 2010, the JRS Board of Directors, December 2010, and the ALAT Executive Committee, November 2010

RECOMMANDATIONS

Recommandations pratiques pour le diagnostic et la prise en charge de la fibrose pulmonaire idiopathique. Élaborées par le centre national de référence et les centres de compétence pour les maladies pulmonaires rares sous l'égide de la Société de pneumologie de langue française

French practical guidelines for the diagnosis and management of idiopathic pulmonary fibrosis. From the National Reference and the Competence centers for rare diseases and the Société de Pneumologie de Langue Française

V. Cottin[a,*], B. Crestani[b], D. Valeyre[c], B. Wallaert[d], J. Cadranel[e], J.C. Dalphin[f], P. Delaval[g], D. Israel-Biet[h], R. Kessler[i], M. Reynaud-Gaubert[j], J.F. Cordier[a], B. Aguilaniu[k], B. Bouquillon[l], P. Carré[m], C. Danel[n], J.-B. Faivre[o], G. Ferreti[p], N. Just[q], S. Kouzan[r], F. Lebargy[s], S. Marchand Adam[t], B. Philippe[u], G. Prévot[v], B. Stach[w], F. Thivolet-Béjui[x]

Consensus ATS/ERS/JRS/ALAT 2011
Recommandations SPLF 2014

Recommandation	Traitement	Niveau de preuve*
Fortement pour	**Oxygénothérapie**	**+**
	Transplantation pulmonaire	**++**
Faiblement pour	Réhabilitation respiratoire	++
	Corticostéroïdes pour les EA	+
	Traitement du RGO asymptomatique	+

* Very low-quality evidence : +
Low-quality evidence : ++
Moderate quality-evidence: +++
High quality-evidence: ++++

Recommandation	Traitement	Niveau de preuve*
Fortement contre	Cs en monothérapie	+
	Colchicine	+
	Cyclosporine A	+
	Combinaison Cs et IS	++
	Interféron γ-1b	++++
	Bosentan	+++
	Etanercept	+++
Faiblement contre	**Combinaison NAC-CS-AZT**	++
	NAC monothérapie	++
	Anticoagulants	+
	Pirfenidone	++ à +++
	Ventilation mécanique	++
	Anti-hypertenseurs pour l'HTP associée	+

Traitements sans recommandations:

- **BIBF 1120**
- Sildenafil Anstrom et al. *N Engl J Med* 2010
- Imatinib Daniels et al. *AJRCCM* 2010
- Macitentan Raghu et al. *Eur Respir J* 2013
- Ambrisentan Raghu et al. *Ann Inter Med* 2013

Recommandation	Traitement	Niveau de preuve*
Fortement contre	Cs en monothérapie	+
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	Anticoagulants	+
	Pirfenidone	++ à +++
	Ventilation mécanique	++
	Anti-hypertenseurs pour l'HTP associée	+

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- Ambrisentan Raghu et al. *Ann Inter Med* 2013

between patients taking acetylcysteine and those taking placebo, exc
cantly lower rate of myelotoxic effects in the group taking acetylcystei

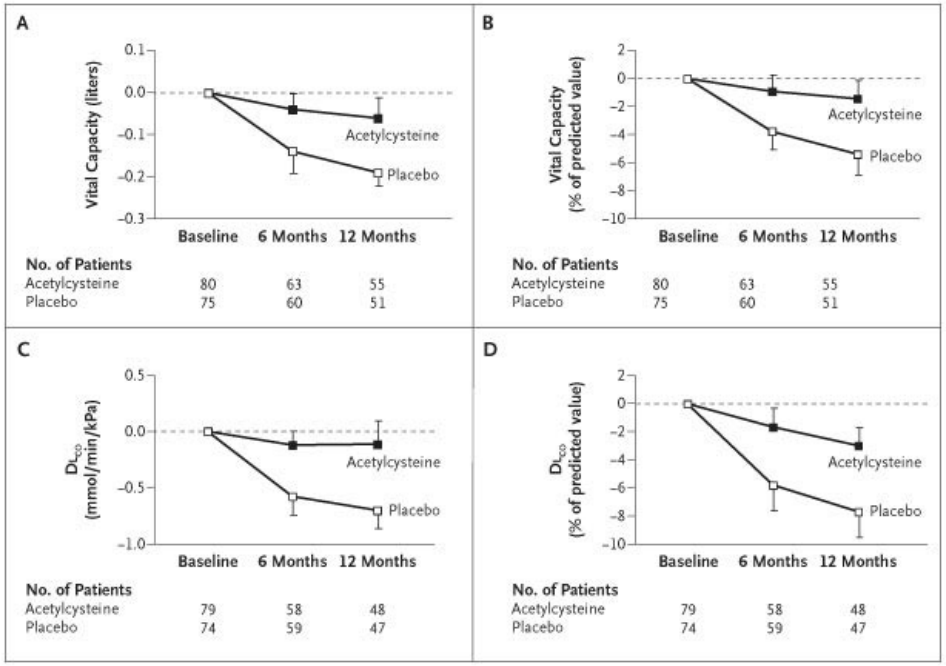
CONCLUSIONS

Therapy with acetylcysteine at a dose of 600 mg three times daily, add
and azathioprine, preserves vital capacity and DL_{CO} in patients with id
nary fibrosis better than does standard therapy alone.

N ENGL J MED 353;21 WWW.NEJM.ORG NOVEMBER 24, 2005

Prednisone + AZT

- + NAC: 600mg x 3/j
- ou Placebo



≠ relative: 9%
p=0.02

≠ relative: 24%
p=0.003

PANTHER-IPF: Prednisone + AZT + NAC vs NAC seul vs Placebo

Serious adverse event — no. (%)	24 (31)	8 (10)	
Based on Kaplan–Meier estimate at 60 wk — % (95% CI)			
Death from any cause	19.8 (9.9–37.2)	2.0 (0.3–13.6)	9.26 (1.1[illegible]–
Death from any cause or hospitalization	43.6 (30.7–59.0)	16.9 (8.7–31.5)	3.74 (1.68–[illegible]
Death from any cause or ≥10% decline in FVC	36.3 (23.7–53.0)	32.4 (19.7–50.3)	1.46 (0.70–[illegible]

* FVC denotes forced vital capacity.

- Arrêt du bras combination-therapy
- Comparaison des groupes NAC seul et placebo en cours

This article has an online supplement, which is accessible from this issue's table of contents online at www.atsjournals.org

Am J Respir Crit Care Med Vol 171. pp 1040–1047, 2005
Originally Published in Press as DOI: 10.1164/rccm.200404-571OC on January 21, 2005
Internet address: www.atsjournals.org

ratory crackles, abnormal PFTs (1), and increased s
damaged-pneumocyte markers (KL-6 [29] and surfactant
D [30]), was required in addition. Eligible patients were
of age with adequate oxygenation at rest ($Pa_{O_2} \geqslant 70$

usual interstitial pneumonia (UIP) was p
not in accordance with the predetermin
col (see online supplementary material)

For editorial comments see page 728.

treatments, provides a strong rationale for the development of novel drugs that target the underlying fibroproliferative process and attenuate decline in pulmonary function.

double-blind, placebo-107 Japanese patient fibrosis.[13] This study

Design

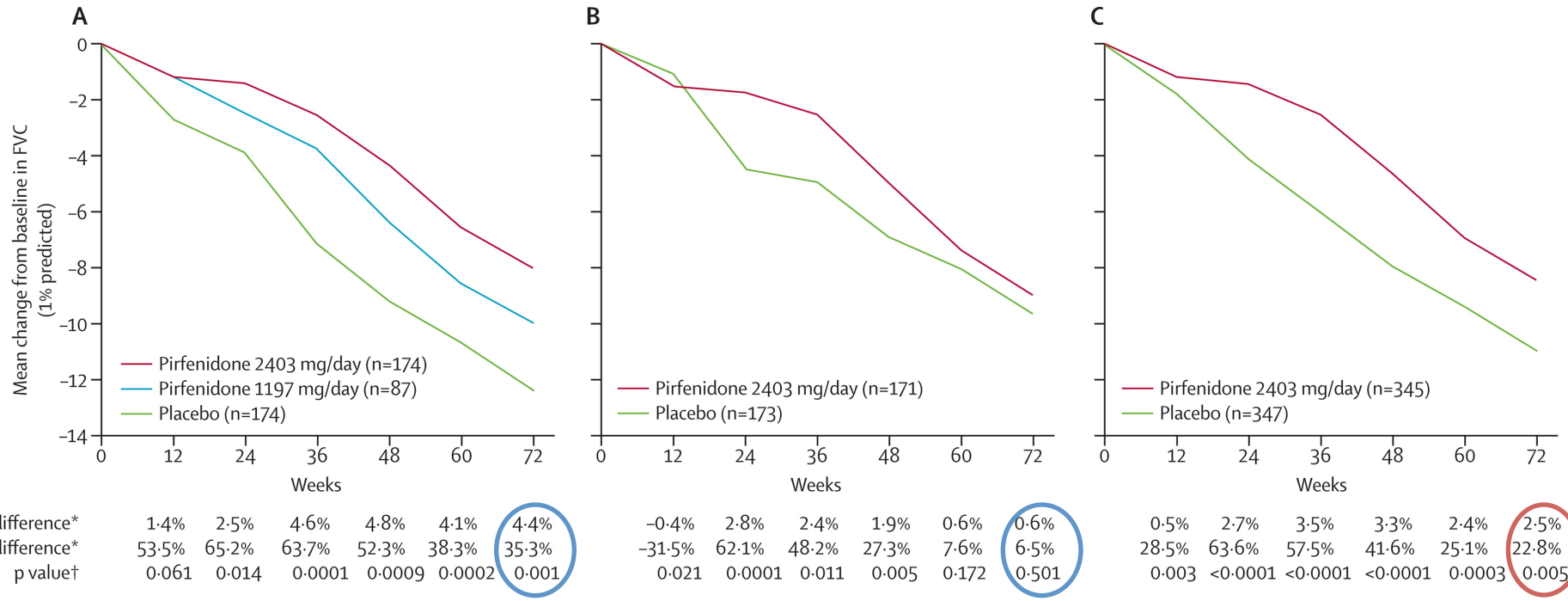
- Étude randomisée en double insu vs placebo, multicentrique internationale
- n=779 patients

Objectif principal

CVF à 72 semaines

CAPACITY 1	CAPACITY2
N=344	N= 435
Posologie: 2403 mg	Posologie forte: 2403 mg Posologie faible: 1197 mg

Variation CVF à 72 semaines

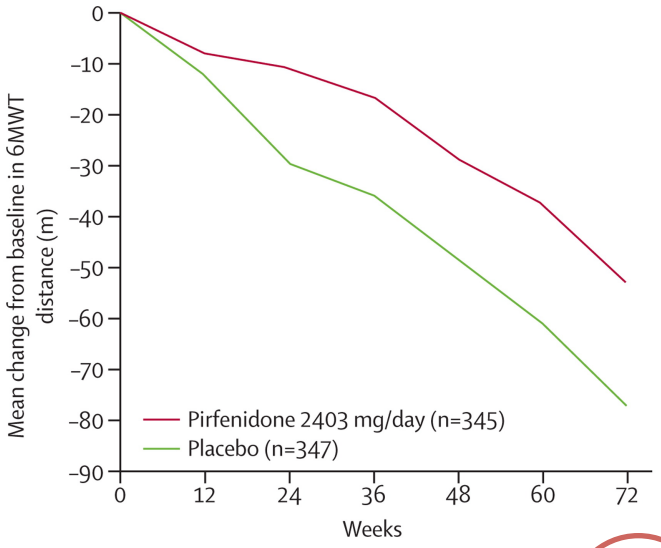


Absolute difference*	1·4%	2·5%	4·6%	4·8%	4·1%	4·4%
Relative difference*	53·5%	65·2%	63·7%	52·3%	38·3%	35·3%
p value†	0·061	0·014	0·0001	0·0009	0·0002	0·001

Absolute difference*	−0·4%	2·8%	2·4%	1·9%	0·6%	0·6%
Relative difference*	−31·5%	62·1%	48·2%	27·3%	7·6%	6·5%
p value†	0·021	0·0001	0·011	0·005	0·172	0·501

Absolute difference*	0·5%	2·7%	3·5%	3·3%	2·4%	2·5%
Relative difference*	28·5%	63·6%	57·5%	41·6%	25·1%	22·8%
p value†	0·003	<0·0001	<0·0001	<0·0001	0·0003	0·005

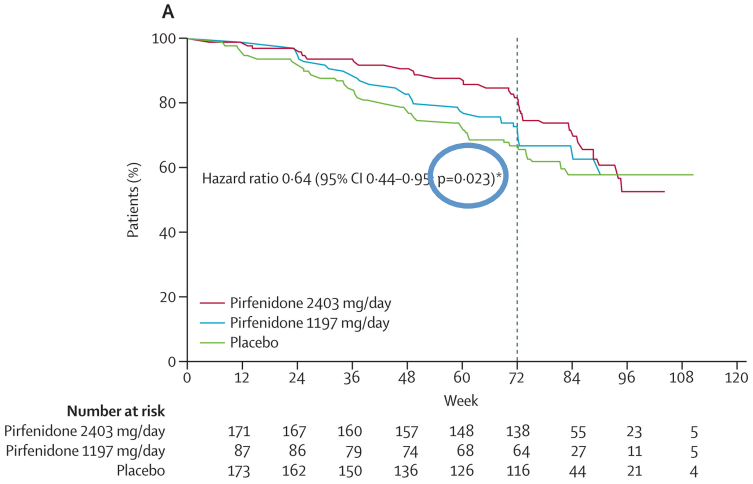
Variation distance TM6' à 72 semaines

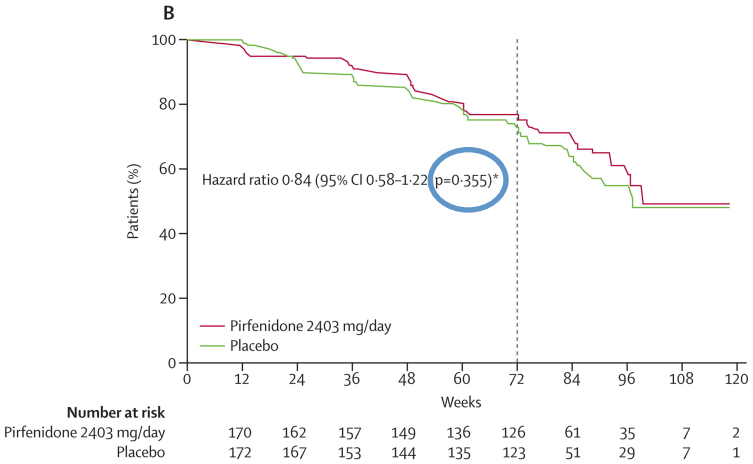


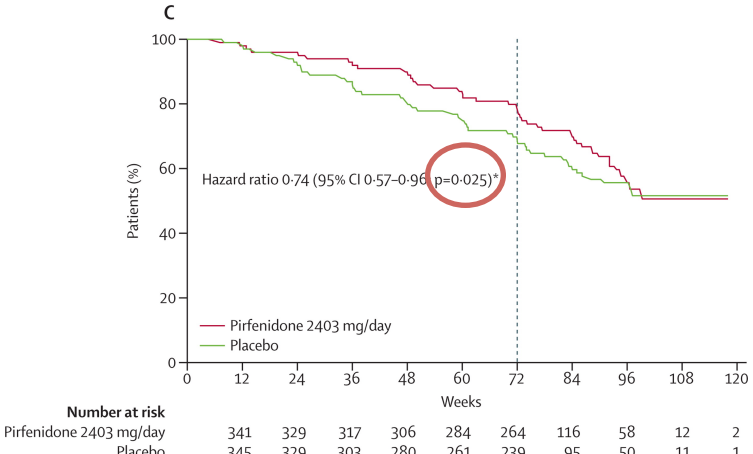
Absolute difference* (m)	3·9	18·6	18·7	19·8	23·3	24·0
Relative difference*	32·2%	62·8%	52·5%	40·6%	38·2%	31·2%
p value†	0·760	0·042	0·053	0·004	0·002	0·0009

Incidence des EA ?

Survie sans progression







Effets secondaires

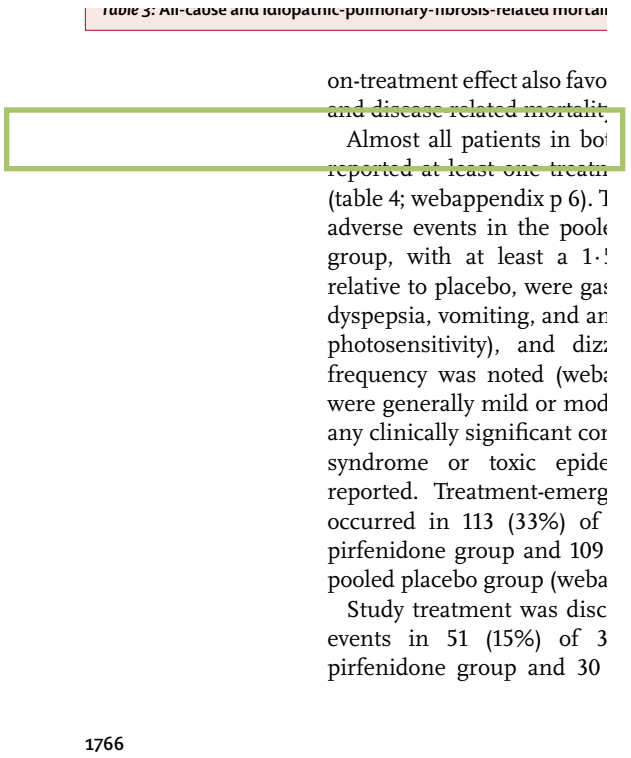


Table 3: All-cause and idiopathic-pulmonary-fibrosis-related mortali

on-treatment effect also favo
and disease-related mortalit
Almost all patients in bo
reported at least one treatm
(table 4; webappendix p 6). T
adverse events in the pool
group, with at least a 1·
relative to placebo, were ga
dyspepsia, vomiting, and ar
photosensitivity), and diz
frequency was noted (web
were generally mild or mod
any clinically significant cor
syndrome or toxic epide
reported. Treatment-emerg
occurred in 113 (33%) of
pirfenidone group and 109
pooled placebo group (weba
Study treatment was disc
events in 51 (15%) of 3
pirfenidone group and 30

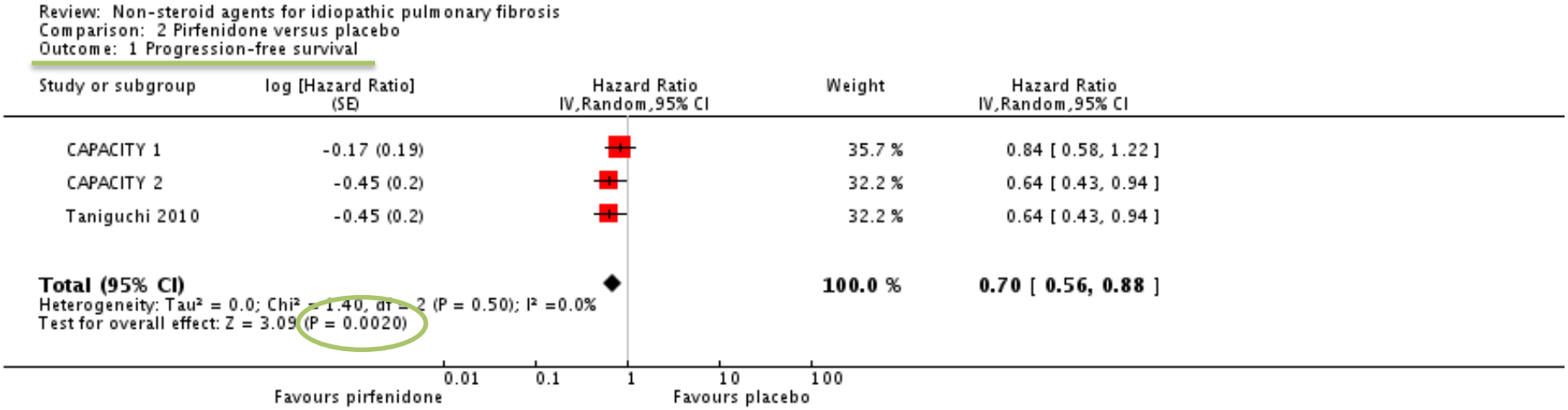
1766

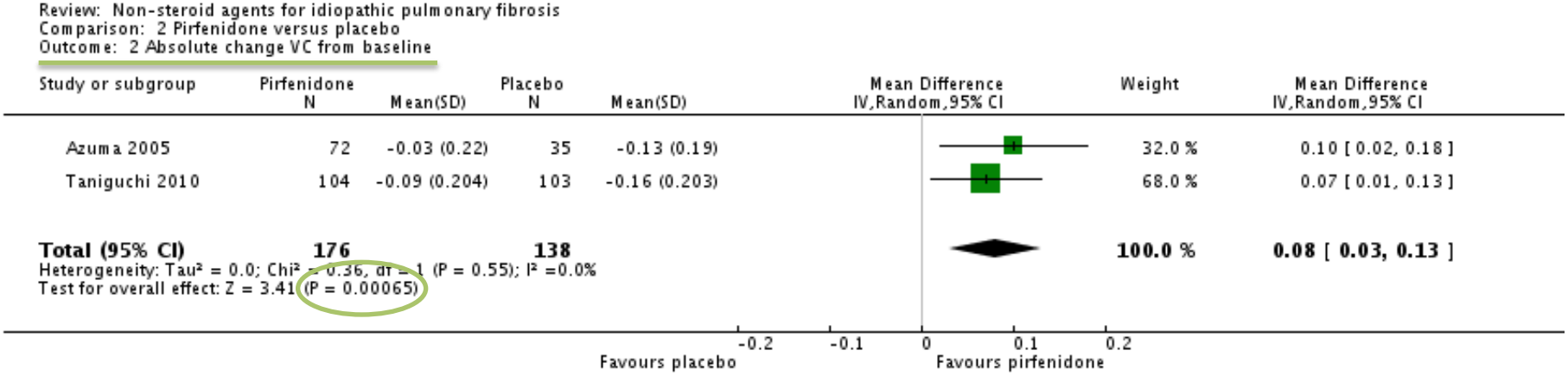
- Tt arrêté pour effets 2^{aires} dans 15% (rash, nausées)
- Pas de différence significative sur la fréquence des SAE (15% vs 9%)

Non-steroid agents for idiopathic pulmonary fibrosis (Review)

Spagnolo P, Del Giovane C, Luppi F, Cerri S, Balduzzi S, Walters EH, D'Amico R, Richeldi L

THE COCHRANE COLLABORATION®





daily, as compared with placebo, was associated with a trend toward a reduction in the decline in lung function, with fewer acute exacerbations and preserved quality of life. (Funded by Boehringer Ingelheim; ClinicalTrials.gov number, NCT00514683.)

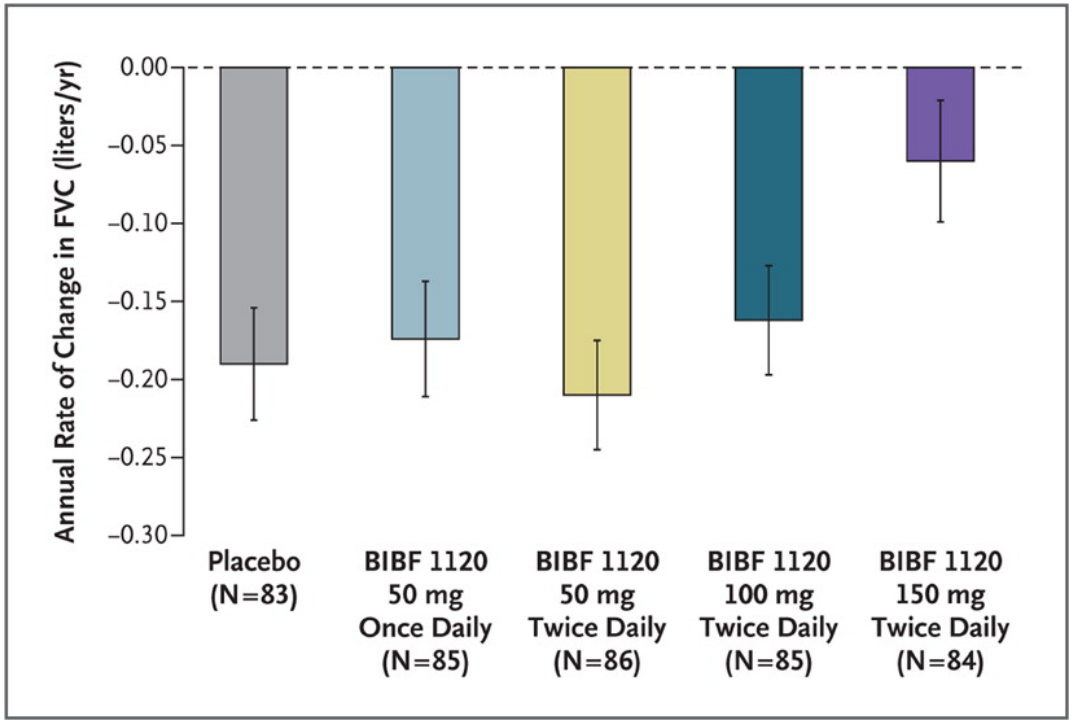
N ENGL J MED 365;12 NEJM.ORG SEPTEMBER 22, 2011

Design

- Étude randomisée en double insu vs placebo, multicentrique internationale
- Patients:
  - BIBF 1120: 50 mg/j (n=86) ou 50mg x 2/j (n=86) ou 100 mg x2/j (n=86) ou 150 mg x 2/j (n=85)
  - Placebo (n=85)

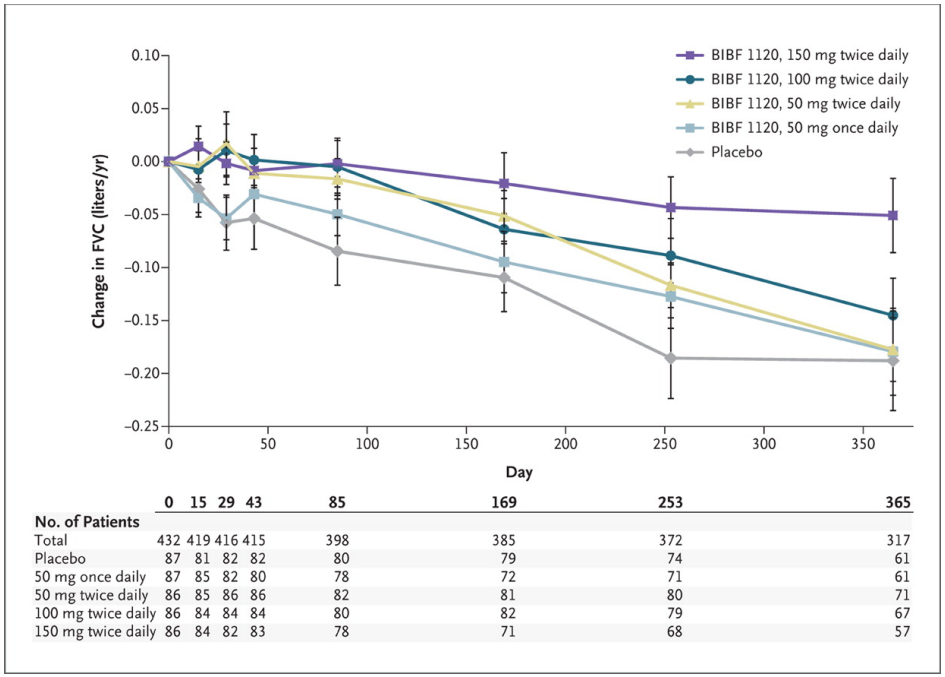
Objectif principal

CVF à 12 mois



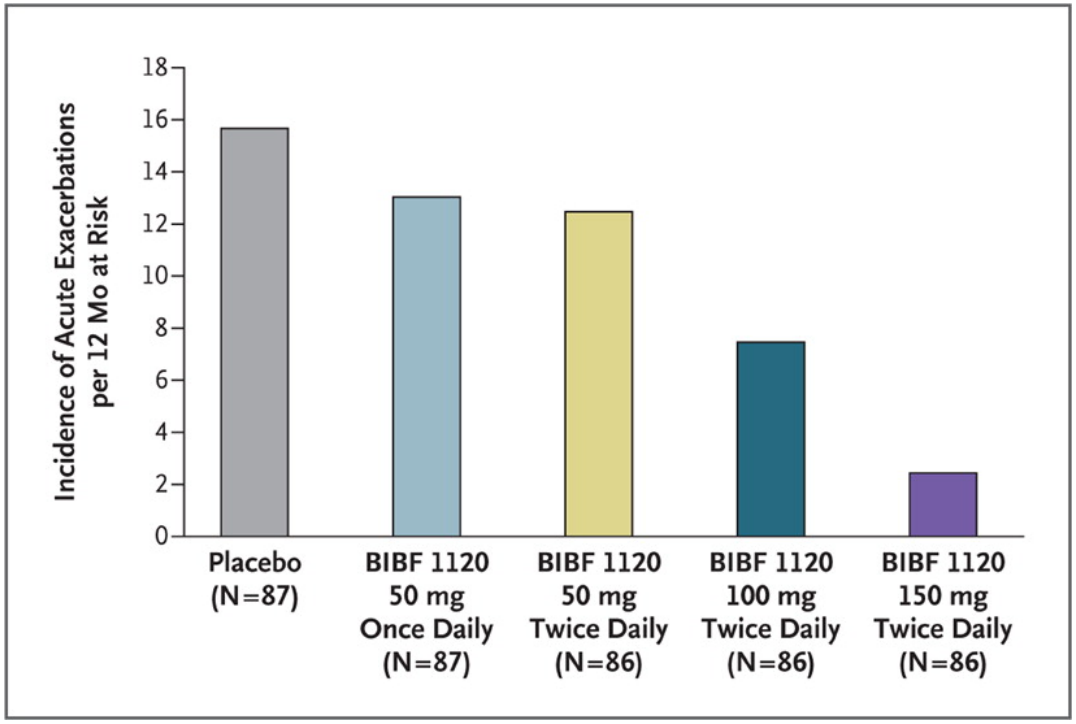
Variation CVF à 12 mois

p = 0.06 ou 0.01
Réduction de 68.4% du déclin annuel



	0	15	29	43	85	169	253	365
No. of Patients								
Total	432	419	416	415	398	385	372	317
Placebo	87	81	82	82	80	79	74	61
50 mg once daily	87	85	82	80	78	72	71	61
50 mg twice daily	86	85	86	86	82	81	80	71
100 mg twice daily	86	84	84	84	80	82	79	67
150 mg twice daily	86	84	82	83	78	71	68	57

Incidence EA



2.4% vs 15.7% (p = 0.02)

Effets secondaires

Cardiac disorders	6 (7.1)	2 (2.3)	2 (2.3)	1 (1.2)	0	11 (2

* Adverse events defined as most frequent were those having an incidence of more than 10% in any study group.

comes, suggesting that this agent is a promising treatment for idiopathic pulmonary fibrosis, a serious medical condition for which there are few therapeutic options.

Although the higher number of discontinuations and dose reductions in the group of patients receiving 150 mg twice a day could have introduced bias in the estimates of treatment effect, the results of sensitivity analyses for the decline in FVC, with discontinuations and dose reductions taken into consideration, were similar to the results of the primary analysis. These observations suggest that the early withdrawal of patients in the group receiving 150 mg of BIBF 1120 twice a day and for whom no follow-up data on FVC were available did not skew our observed outcomes.

The results of secondary end-point analyses provide consistent support for the dose of 150 mg of BIBF 1120 twice a day, and for some end points, the data are strengthened by similar resul the dose of 100 mg twice a day. The incide acute exacerbations was significantly lower group receiving 150 mg twice a day than placebo group. This result is clinically impo since acute exacerbations are associated with disease progression, a severe and abrupt d in FVC, and high mortality.[19,20] The reduct acute exacerbations in patients receiving 1(twice a day or 150 mg twice a day may hav tributed to the more stable quality of life s these groups as compared with the other g which had higher incidences of exacerbation larger numbers of patients with a clinically ingful improvement in the SGRQ score i group receiving 100 mg twice a day and the receiving 150 mg twice a day suggest that ment with BIBF 1120 provided a benefit wi spect to the health-related quality of life, a

Anticoagulant Therapy for Idiopathic Pulmonary Fibrosis*

Hiroshi Kubo, MD, FCCP; Katsutoshi Nakayama, MD; Masaru Yanai, MD; Tomoko Suzuki, MD; Mutsuo Yamaya, MD; Mika Watanabe, MD; and Hidetada Sasaki, MD, PhD

(CHEST 2005; 128:1475–1482)

Pred : 0.5-1 mg/kg/j x 4 sem puis décroissance jusqu'à 10-20 mg/j
n=33

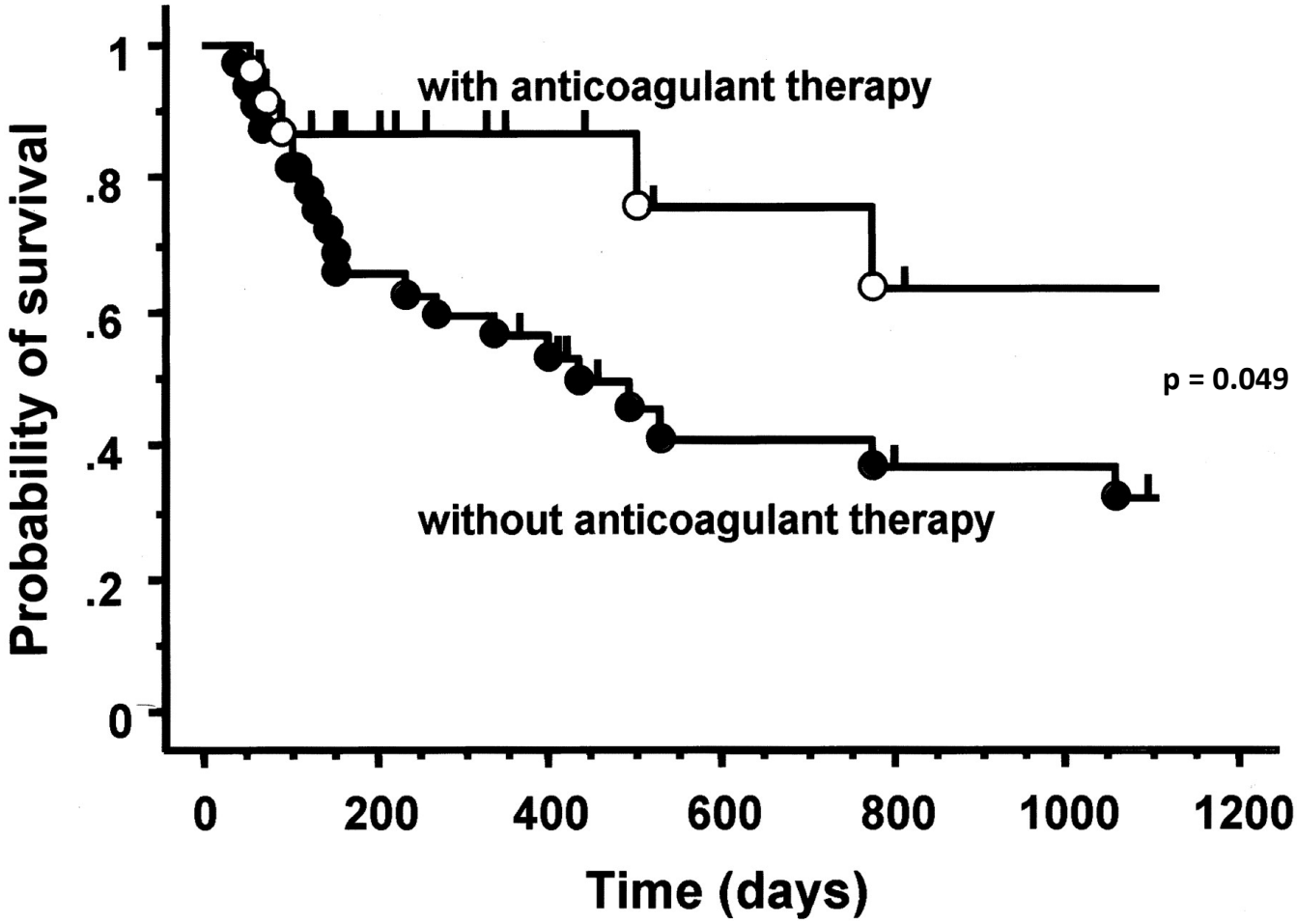
Pred : idem
+ Warfarine PO : INR 2 à 3
n=23

Suivi médian : 12.4 mois

Hospitalisation pour IRA : 60%
- EA : 72.5%
- Autres causes

- EA : Methylpred 500-1000mg/j x 3j
- Traitement cause

Daltéparine IV : 75UI/kg/j x 1-2 sem
- EA : Methylpred 500-1000mg/j x 3j
- Traitement cause



- Mortalité liée à l'EA significativement moins élevée dans le groupe anticoagulant (2/11 vs 15/21, p=0.008)
- Héparine possiblement efficace sur l'EA ?

Am J Respir Crit Care Med Vol 186, Iss. 1, pp 88–95, Jul 1, 2012

Originally Published in Press as DOI: 10.1164/rccm.201202-0314OC on May 3, 2012
Internet address: www.atsjournals.org

spiratory Society, and Latin American Thoracic
guidelines includes anticoagulation as a choice for
of patients, despite remaining uncertainty regarding
and harms (1).

Design

• Étude randomisée en double insu vs placebo, multicentre, américaine

• Patients

- Warfarine: objectif d'INR: 2-3 (n=72)
- Vs placebo (n=73)

• Pendant 48 semaines

Objectif principal

Composite (survie, hospitalisation non liée à un saignement, déclin CVF > 10%)

tion and all-cause mortality ($P = 0.034$) (Figure 2C).

Safety and Secondary Endpoints

There were no significant treatment effects observed in the physiologic secondary endpoints (FVC, 6-minute walk distance,

not appear to be explained by baseline imbalances or infl
by individual centers, and, if proven true, worsening of r
tory status by warfarin is an entirely novel consequence
therapy.

Point-of-care INR monitoring has been used in prior tr
our knowledge, this is the first clinical trial to doubl

Respiratory: IPF	No	18	33	
Cardiovascular: myocardial infarction	No	43	61	
Cardiovascular: sudden cardiovascular death	No	36	53	
Respiratory: IPF	No	27	43	
Respiratory: IPF	No	18	37	
Respiratory: respiratory failure	No	44	86	
Cardiovascular: sudden cardiovascular death	No	25	48	
Respiratory: respiratory failure	No	8	39	
Respiratory: IPF	Yes	17	44	
Respiratory: IPF	Yes	21	58	
Respiratory: IPF	Yes	17	37	
Respiratory: pneumonia	Yes	36	53	
Summary	4	25.1 ± 11.06	50.3 ± 15.51	70.9
Placebo				
Respiratory: IPF	No	18	53	
Respiratory: IPF	No	12	39	
Respiratory: respiratory failure	Yes	16	34	
Summary	1	15.3 ± 3.06	42.0 ± 9.85	71.3

Definition of abbreviations: D_{LCO} = carbon monoxide diffusion capacity; IPF = idiopathic pulmonary fibrosis.

- Arrêt prématurée de l'étude

Treating idiopathic pulmonary fibrosis with the addition of co-trimoxazole: a randomised controlled trial

Ludmila Shulgina,[1] Anthony P Cahn,[2] Edwin R Chilvers,[3] Helen Parfrey,[3] Allan B Clark,[1] Edward C F Wilson,[1] Orion P Twentyman,[4] Anthony G Davison,[5] John J Curtin,[4] Michael B Crawford,[4] Andrew M Wilson[1,4]

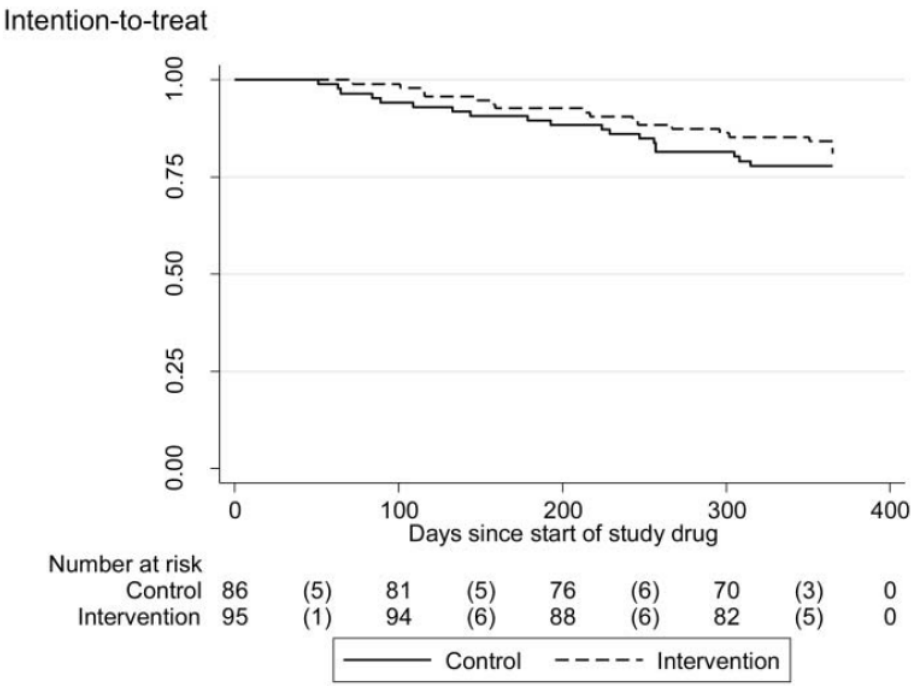
Thorax 2013;**68**:155–162.

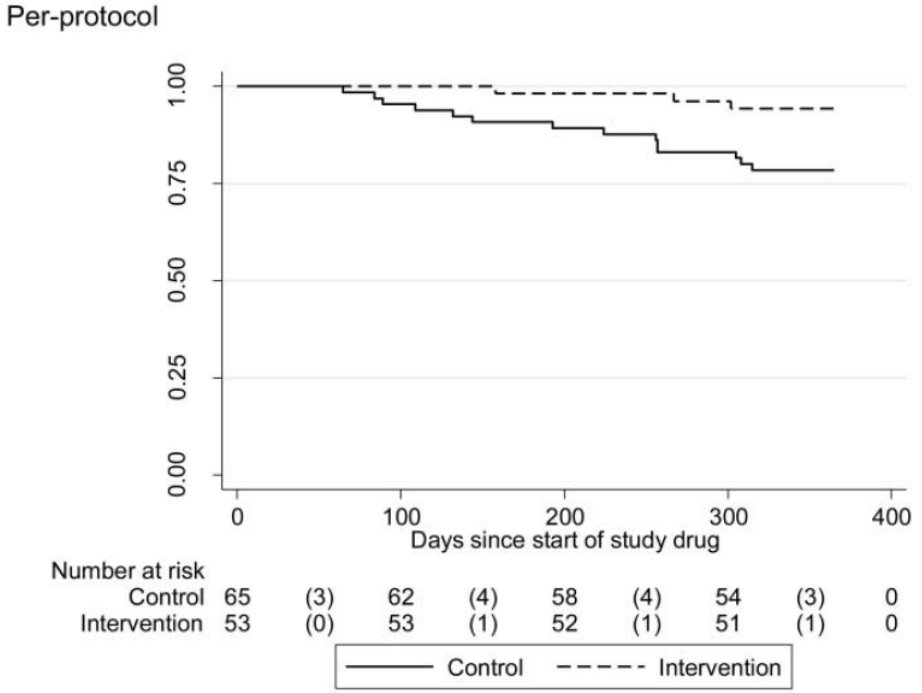
Design

- Étude randomisée en double insu vs placebo, multicentre, anglaise
- Patients: FPI (n=170) et PINS (n=11)
  - Cotrimoxazole: 960 mg x 2/j (n=95)
  - Vs placebo (n=86)
- Patients traités par IS (prednisone, AZT ou MMF), du NAC ou une détérioration EFR

Objectif principal

Variation CVF à 12 mois





Mortalité
5.7% vs 21.5% (HR : 0.21 [IC95% : 0.06-0.78], p=0.02)

- Mortalité significativement plus élevée chez les patients recevant un IS dans le groupe placebo (p=0.015).
- Incidence moindre des infections: pneumonies (0% vs 9.3%, p=0.002), infections respiratoires basses (29.4 vs 44.2, p=0.04) et infections des VAS (6.5 vs 16.3, p=0.039).

Thalidomide for the Treatment of Cough in Idiopathic Pulmonary Fibrosis

A Randomized Trial

Maureen R. Horton, MD; Victoria Santopietro; Leena Mathew, BS; Karen M. Horton, MD; Albert J. Polito, MD; Mark C. Liu, MD; Sonye K. Danoff, MD; and Noah Lechtzin, MD

Ann Intern Med. 2012;157:398-406.

Design

• Étude randomisée mono-centrique en double-aveugle versus placebo, en cross-over.

• Patients: n=24

- Traitement de 12 semaines avec un wash-out de 2 semaines
- Début: 50 mg/j et augmenté à 100mg/j en cas de persistance de la toux
- 20 patients ont achevé les deux périodes

Objectif principal

Cough Quality of Life Questionnaire

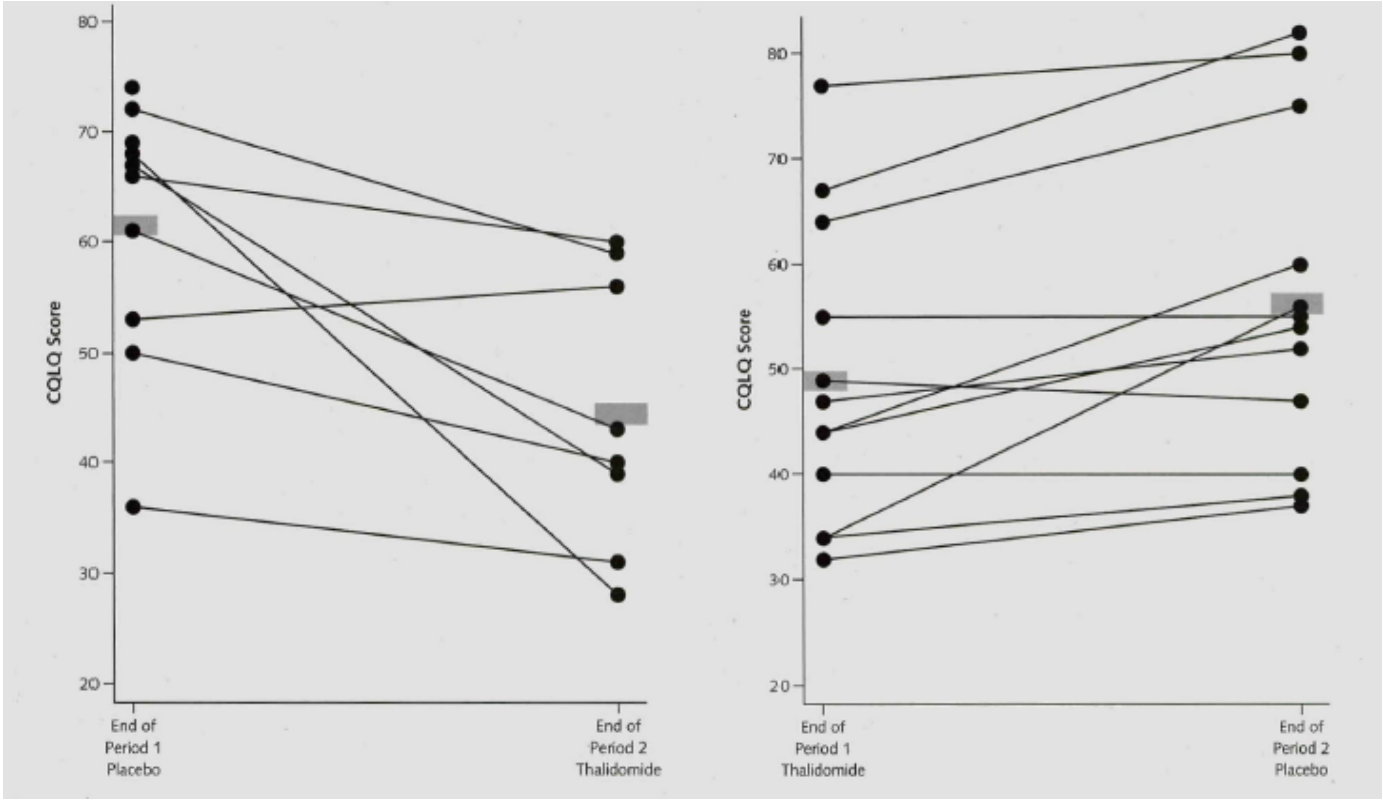
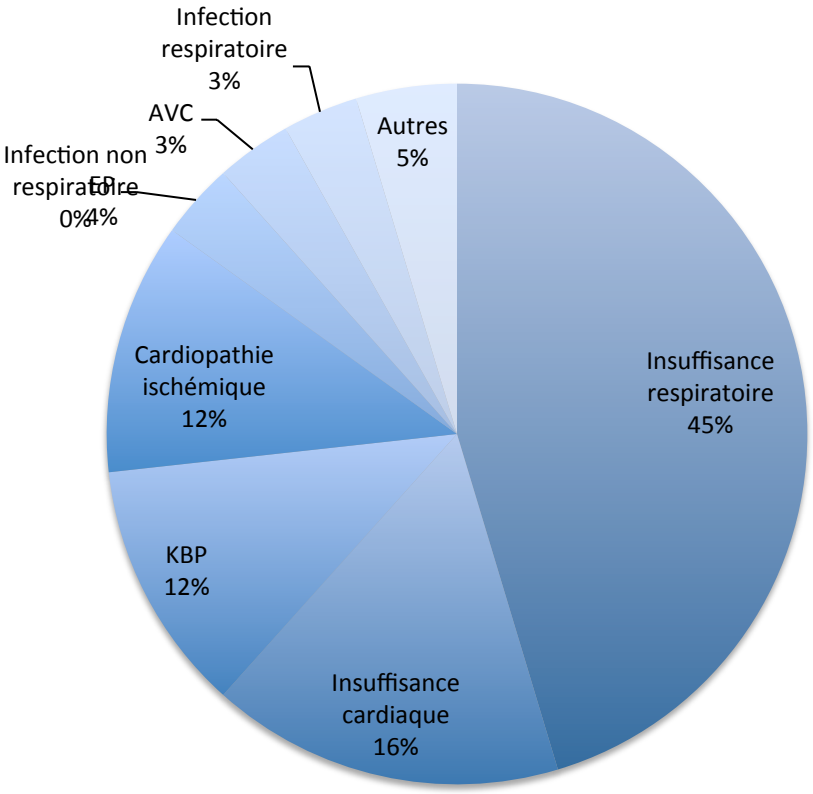


Table 2. **CQLQ, VAS, and SGRQ Scores After Placebo and Thalidomide Treatments***

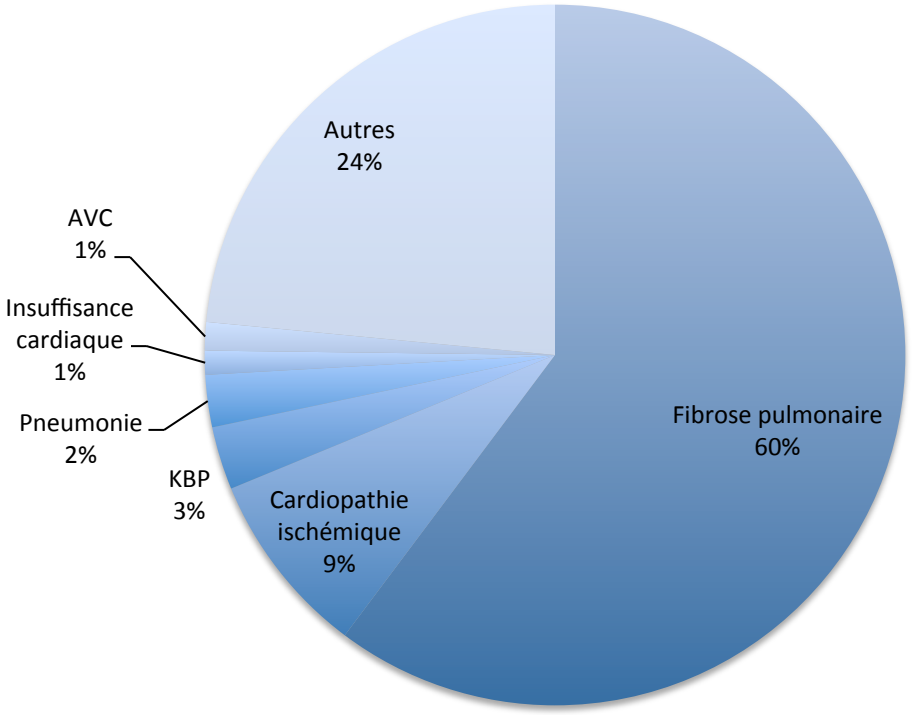
Measure	Mean Score at Baseline (SD)	Mean Score After 12 wk of Placebo (SD)	Mean Score After 12 wk of Thalidomide (SD)	Mean Difference (95% CI)†	*P* Value†
CQLQ	60.5 (12.0)	58.7 (14.0)	47.2 (13.4)	−11.4 (−15.7 to −7.0)	<0.001
Cough VAS	64.8 (21.4)	61.9 (26.5)	32.2 (26.1)	−31.2 (−45.2 to −17.2)	<0.001
SGRQ total	57.4 (18.8)	56.9 (17.1)	43.9 (16.0)	−11.7 (−18.6 to −4.8)	0.001
SGRQ symptom domain	67.7 (19.7)	62.0 (18.3)	50.3 (20.9)	−12.1 (−22.2 to −2.0)	0.018
SGRQ impact domain	48.1 (20.7)	49.0 (19.4)	34.3 (16.1)	−13.1 (−19.7 to −6.6)	<0.001
SGRQ activity domain	64.3 (22.7)	65.8 (18.7)	60.9 (14.2)	−3.3 (−9.8 to 3.2)	0.31

Effets adverses: 74% vs 22%, p=0 .001 (constipation: 36%, vertiges: 27%, malaises: 14%, anorexie: 5% et bradycardie asymptomatique: 5%)

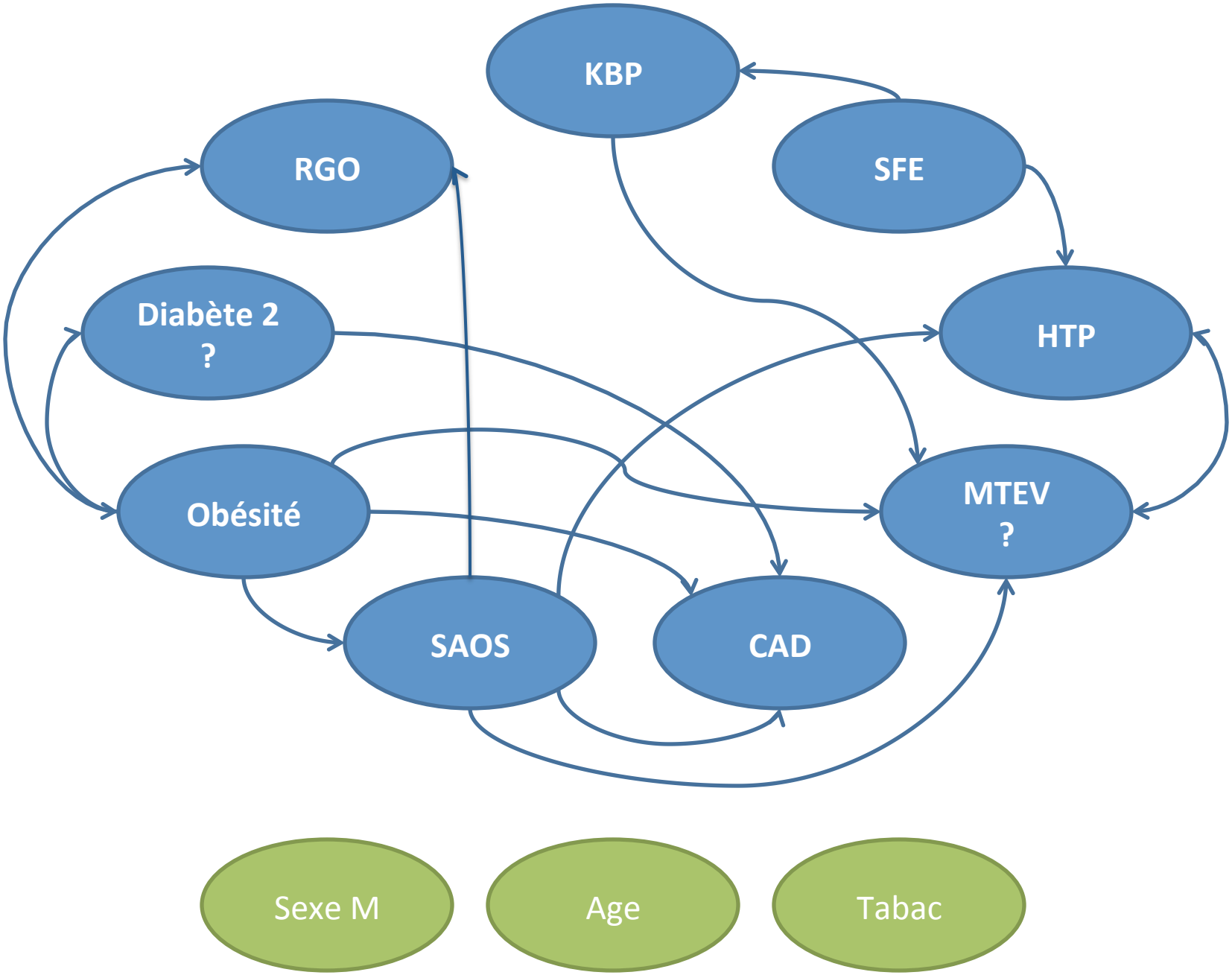
Causes de mortalité



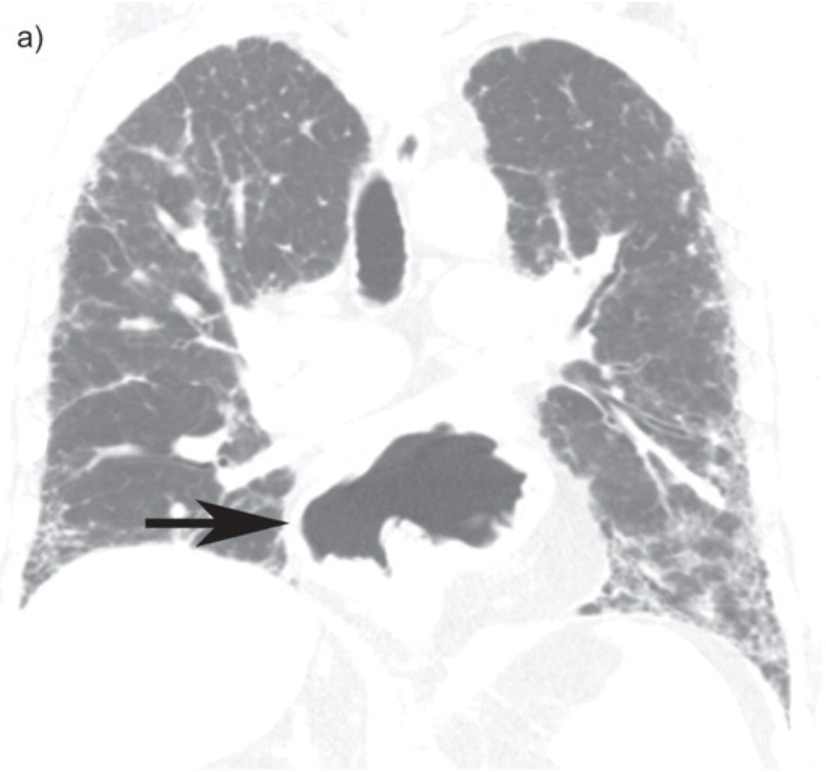
Panos et al. *Am J Med* 2010

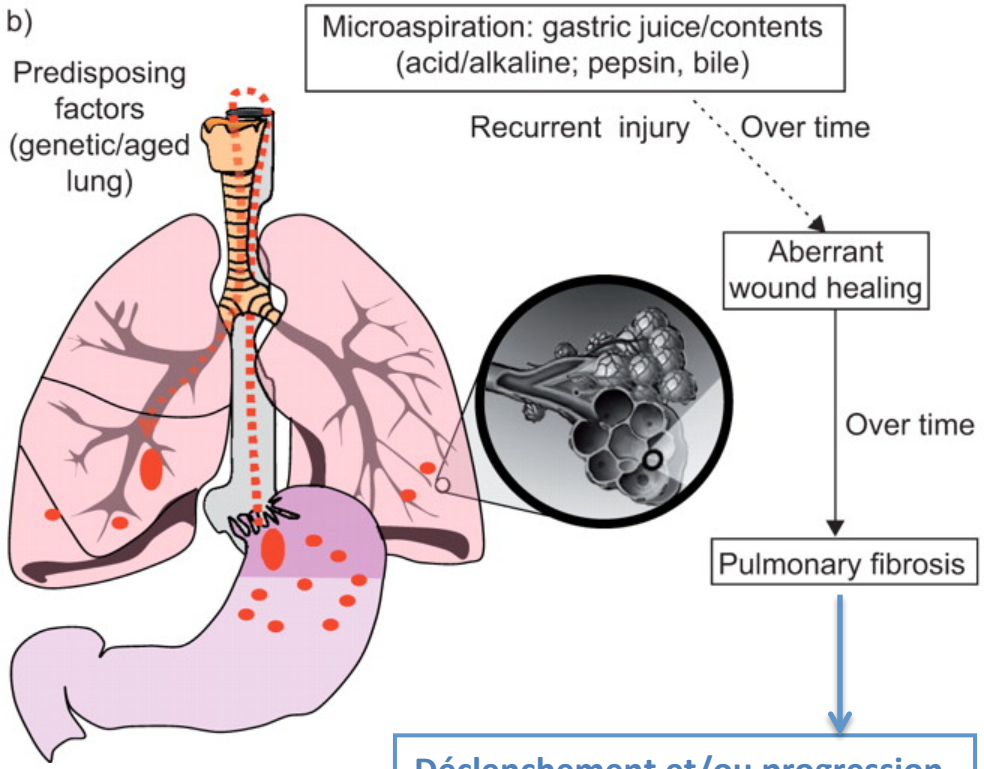


Olson et al. *Am J Respir Crit Care Med* 2007


KBP
RGO
SFE
Diabète 2
?
HTP
Obésité
MTEV
?
SAOS
CAD
Sexe M
Age
Tabac

RGO et FPI





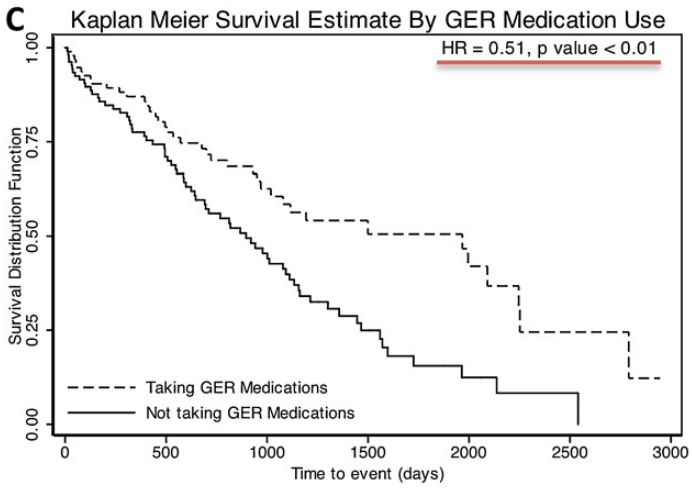
Déclenchement et/ou progression de la fibrose et/ou EA

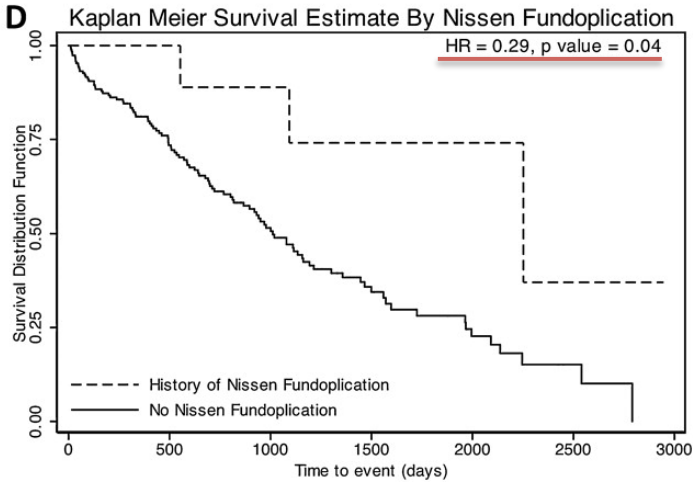
- PH-métrie + : 68%-94.1% des cas de FPI
- > autres PID, asthme, BPCO
- Hernie hiatale: 39%
- 53%-75% asymptomatiques
- Reflux acide sous traitement par IPP: 63%

Tobin et al. *Am J Respir Crit Care Med* 1998
Raghu et al. *Eur Respir J* 2006
Tcherakian et al. *Thorax* 2011
Noth et al. *Eur Respir J* 2012
Lee et al. *Eur Respir J* 2012

Gastroesophageal Reflux Therapy Is Associated with Longer Survival in Patients with Idiopathic Pulmonary Fibrosis

Joyce S. Lee[1], Jay H. Ryu[2], Brett M. Elicker[3], Carmen P. Lydell[3], Kirk D. Jones[4], Paul J. Wolters[1], Talmadge E. King, Jr.[1], and Harold R. Collard[1]





- Étude rétrospective: 204 cas de FPI pris en charge dans 2 centres

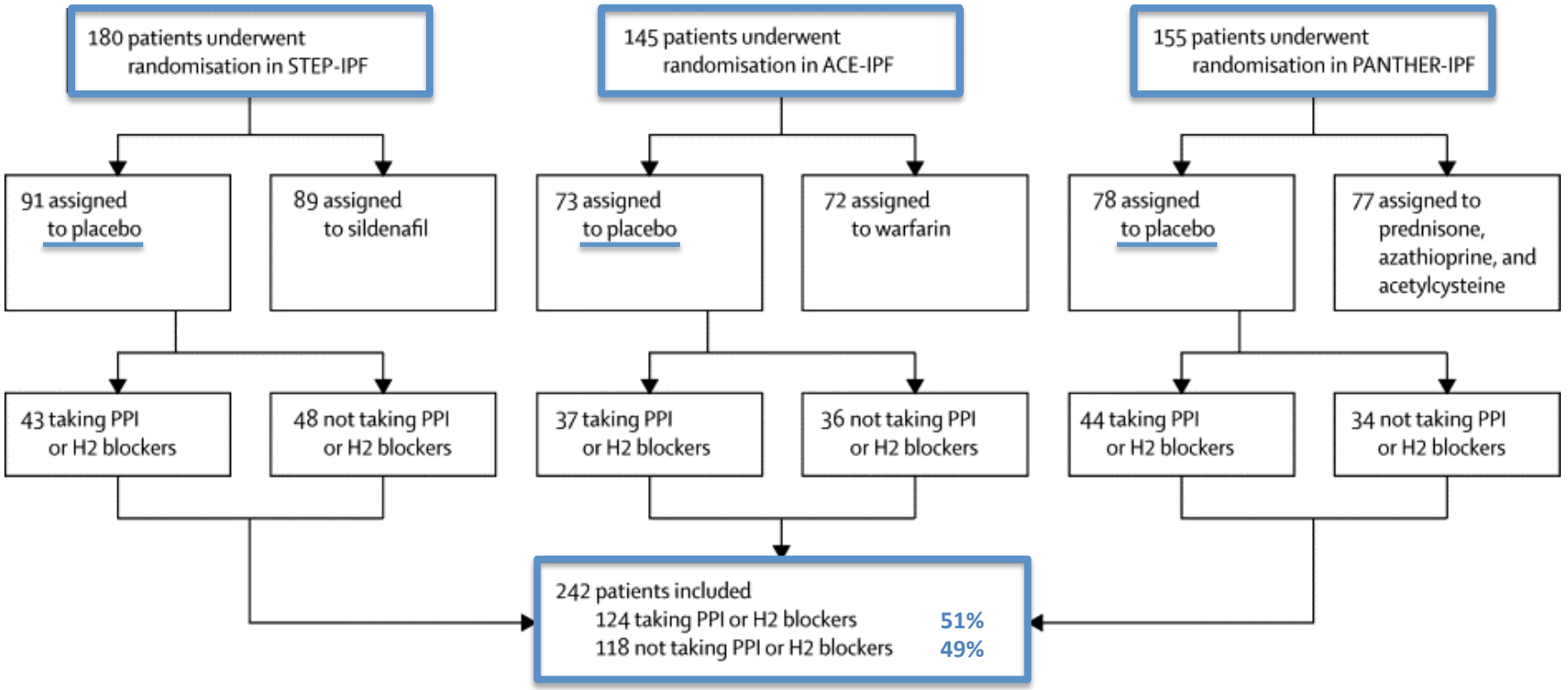
TABLE 3. ADJUSTED PREDICTORS OF SURVIVAL TIME

Variable	HR (95% CI)	*P* Value
Age	1.02 (1.00–1.05)	0.08
Female sex	0.87 (0.54–1.42)	0.58
Long-term oxygen	1.18 (0.72–1.95)	0.65
Prednisone	1.05 (0.61–1.82)	0.85
FVC, % predicted	0.98 (0.96–0.99)	<0.01
D_{LCO}, % predicted	0.98 (0.96–1.00)	0.03
Radiologic fibrosis score, %	1.00 (0.98–1.02)	0.83
Gastroesophageal reflux symptoms*	0.80 (0.45–1.44)	0.46
Gastroesophageal reflux disease†	1.78 (0.90–3.51)	0.10
Gastroesophageal reflux medication use‡	0.47 (0.24–0.93)	0.03
Nissen fundoplication	0.74 (0.21–2.59)	0.64

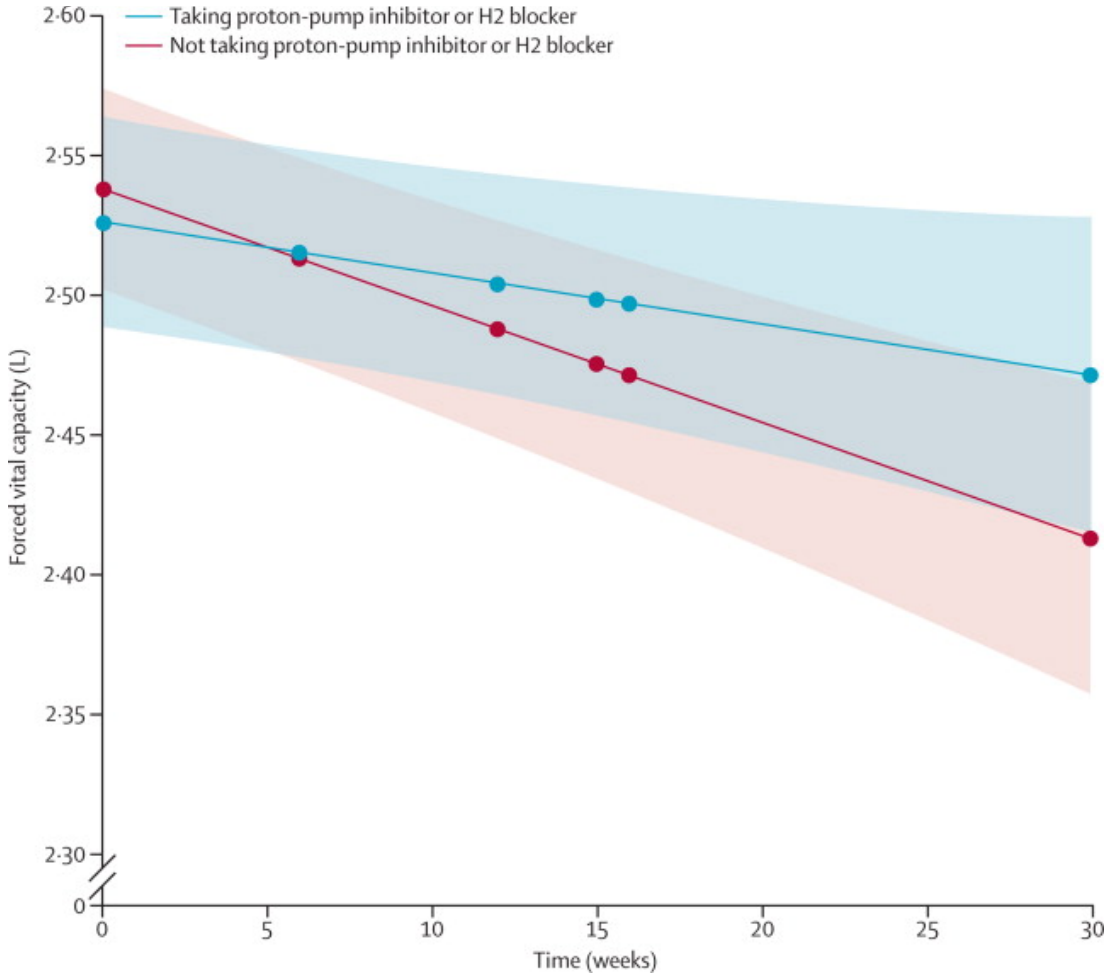
Anti-acid treatment and disease progression in idiopathic pulmonary fibrosis: an analysis of data from three randomised controlled trials

*Joyce S Lee, Harold R Collard, Kevin J Anstrom, Fernando J Martinez, Imre Noth, Rhonda S Roberts, Eric Yow, Ganesh Raghu, for the IPFnet Investigators**

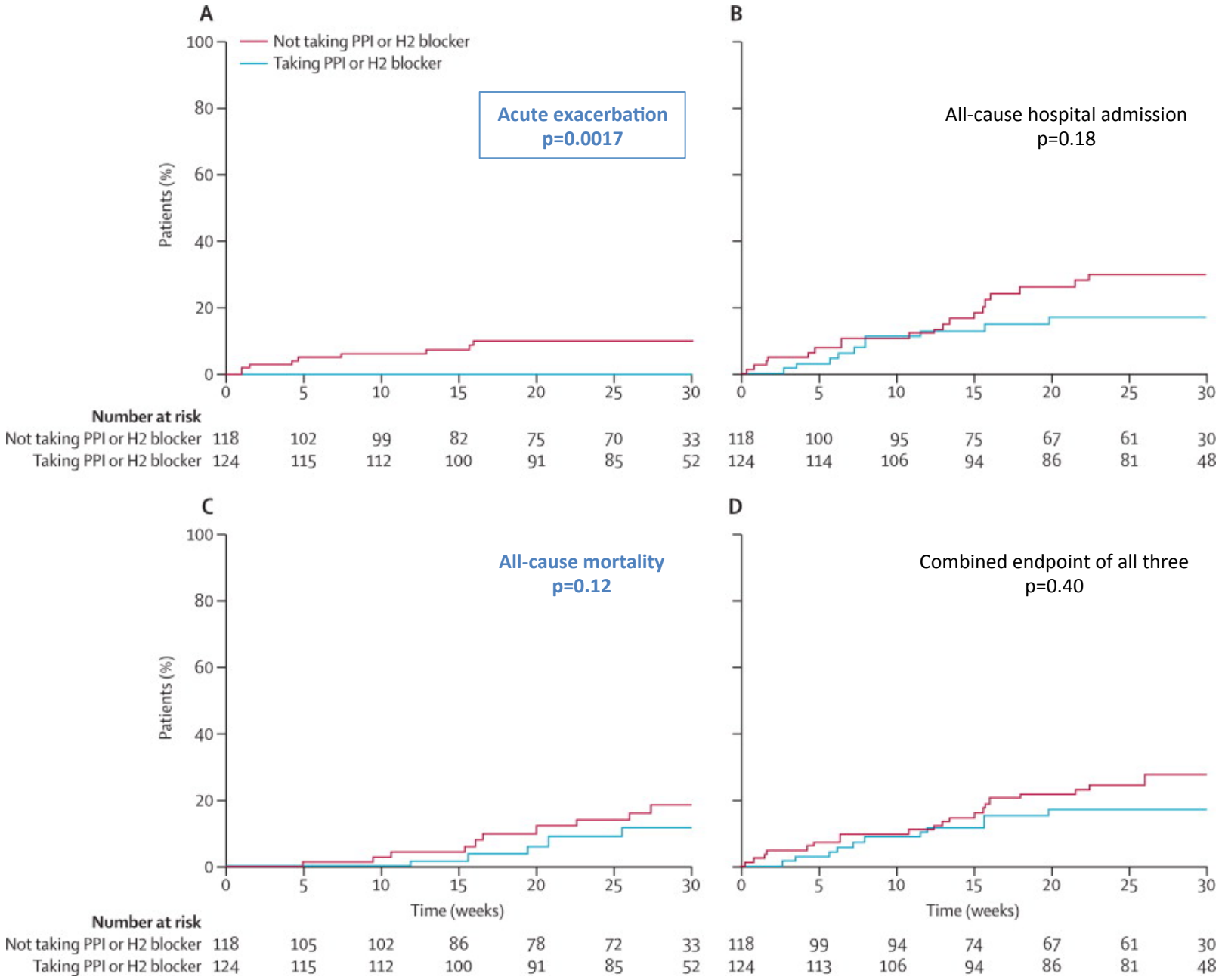
Lancet Respir Med 2013



	Taking PPI or H2 blocker	Not taking PPI or H2 blocker	p value
Comorbidities			
Gastro-oesophageal reflux disease	110/124 (89%)	30/118 (25%)	<0·0001
Barrett's oesophagus¶	9/81 (11%)	1/70 (1%)	0·01
Hiatus hernia¶	24/87 (28%)	2/71 (3%)	<0·0001
Fundoplication surgery	6/124 (5%)	0/118	0·03
Sleep apnoea	46/124 (37%)	16/118 (14%)	<0·0001
Sleep apnoea with continuous positive airway pressure¶	27/123 (22%)	12/118 (10%)	0·01
Asthma	8/124 (6%)	6/118 (5%)	0·65
Diabetes	26/124 (21%)	22/118 (19%)	0·65
Coronary artery disease	32/124 (26%)	22/118 (19%)	0·18
Assessment of abnormal gastro-oesophageal reflux and gastro-oesophageal reflux disease			
Symptoms of heartburn	76/112 (68%)	24/80 (30%)	<0·0001
Barium swallow test	9/112 (8%)	2/80 (3%)	0·06
24 h pH monitoring	17/112 (15%)	1/80 (1%)	<0·0001
Endoscopy	32/112 (29%)	4/80 (5%)	<0·0001
Lifestyle changes to ease symptoms‖	62/112 (55%)	10/80 (13%)	<0·0001
Drugs			
PPI at baseline	113/124 (91%)	0/118	<0·0001
H2 blocker at baseline	11/124 (9%)	0/118	<0·0001
Prednisone	22/124 (18%)	22/118 (19%)	0·86
Prednisone, azathioprine, and acetylcysteine**	7/124 (6%)	6/118 (5%)	0·85



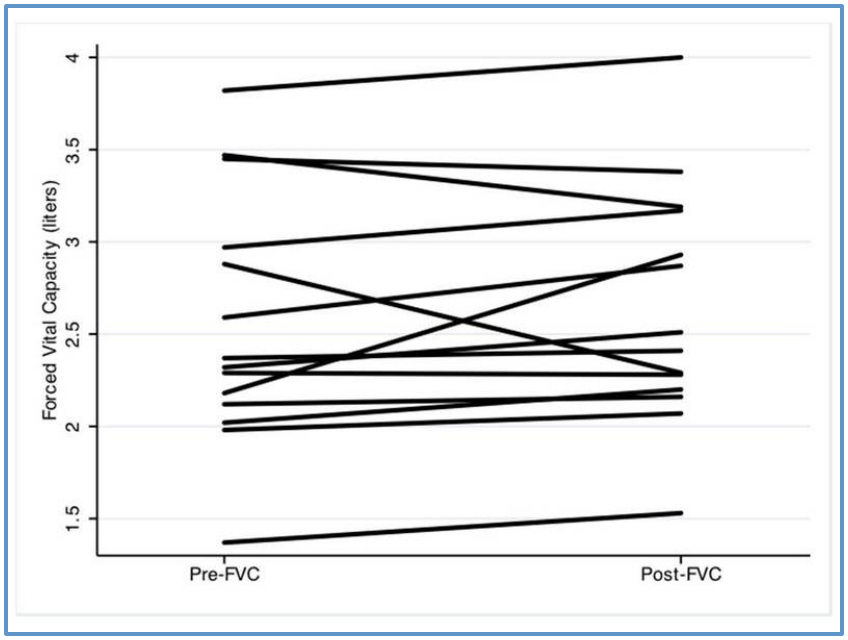
- Déclin CVF: -0.06L (IC95%: -0.11 à -0.01) vs -0.12L (IC95%: -0.17 à -0.08)
- Soit une différence de 0.07L (IC95%: 0 à 0.14), p=0.05
- Y compris après ajustement sur le SAOS et son traitement


A
Not taking PPI or H2 blocker
Taking PPI or H2 blocker
Patients (%)
Acute exacerbation
p=0.0017
B
All-cause hospital admission
p=0.18
Number at risk
Not taking PPI or H2 blocker 118 102 99 82 75 70 33 118 100 95 75 67 61 30
Taking PPI or H2 blocker 124 115 112 100 91 85 52 124 114 106 94 86 81 48
C
All-cause mortality
p=0.12
D
Combined endpoint of all three
p=0.40
Time (weeks)
Number at risk
Not taking PPI or H2 blocker 118 105 102 86 78 72 33 118 99 94 74 67 61 30
Taking PPI or H2 blocker 124 115 112 100 91 85 52 124 113 106 94 86 81 48

Treatment of IPF with laparoscopic anti-reflux surgery is associated with improvement in FVC

Raghu G, Mart D, Anstrom KJ, Hinojosa M, Hayes J, Spada C, Oelschlager B, Pellegrini C

- Série rétrospective monocentrique (Seattle): n=14
- Progression EFR, persistance d'un reflux acide à la pH-métrie malgré un Tt médical et péristaltisme œsophagien non aboli à la manométrie
- Bonne tolérance malgré la fonction altérée - hospitalisation d'une nuit



Gain de **0.08L** (3.5%)
10/14 patients amélioraient leur CVF

Conclusions

- Recommandations thérapeutiques françaises
- Cs et IS non recommandés
- Pirfenidone dans les formes de FPI certaines ou probables, légères à modérées (CVF ≥ 50%, DLCO ≥ 35%) après information du patient
  - Etude **ASCEND** aux EU
  - Etude **PANORAMA** (Pirfénidone + NAC vs Pirfénidone)
- Inclusion dans les essais thérapeutiques: http://clinicaltrials.gov/
  - Etude **RAINIER** et étude **RIFF**
- Comorbidités:
  - Variées
  - Modalités de dépistage et intérêt du Tt à mieux évaluer
  - **Tt anti-reflux:** anti-acides ? prokinétiques ? chirurgie ?
- Ne pas retarder une inscription sur liste de TP et améliorer soins palliatifs

Remerciements

- Equipe de Pneumologie Avicenne: D. Valeyre, Y.Uzunhan, D. Bouvry, O. Freynet, A. Hervé, D. Sadoun
- Equipe de Radiologie Avicenne: M. Brauner, P-Y. Brillet
- Equipe de Physiologie Avicenne: C. Planes, T. Gille
- Equipe d'Anatomo-pathologie Avicenne: M. Kambouchner