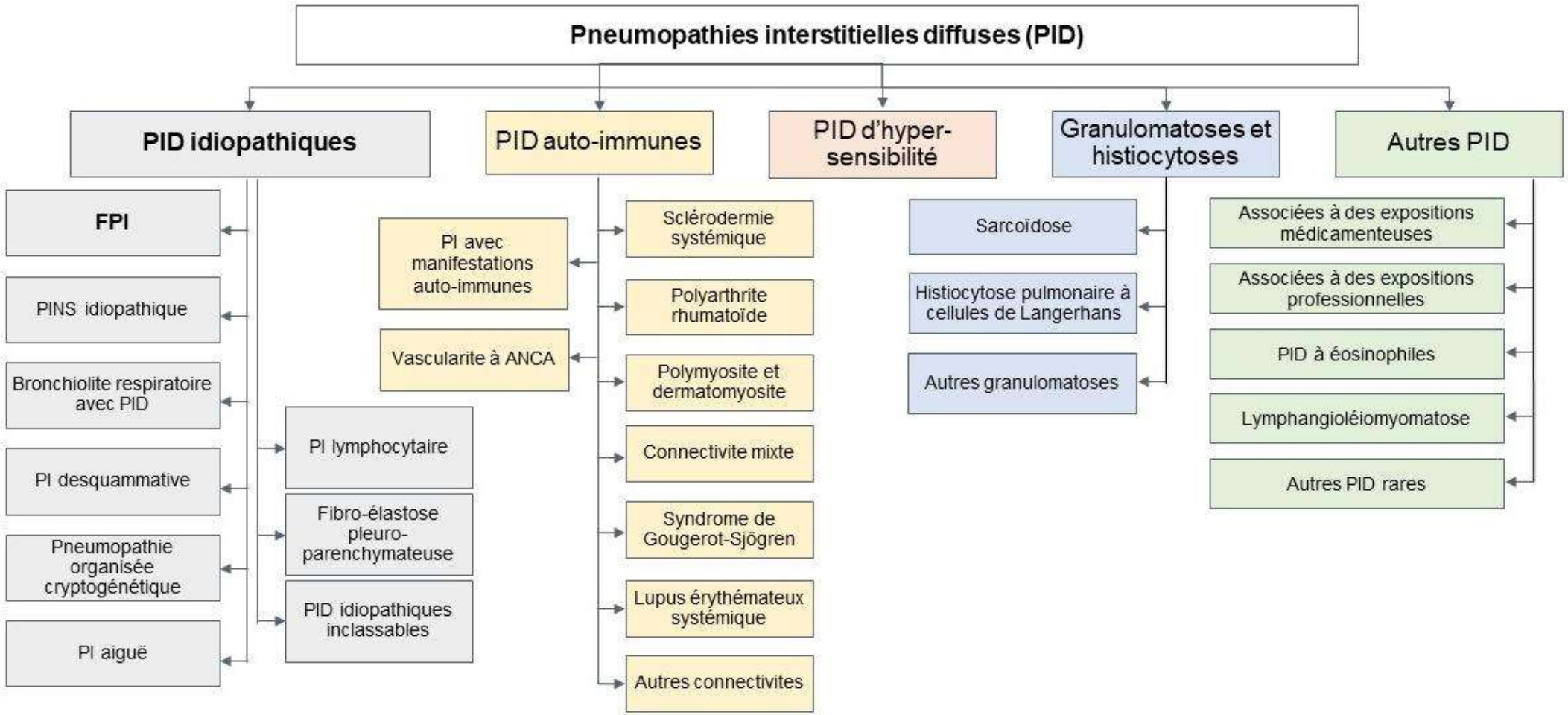
Service de pneumologie
CHU TOULOUSE
Pôle des voies respiratoires

Les Pneumopathies d'Hypersensibilité fibreuses

C Beigelman
G Prévot

Club Thorax 17/09/2021

Classification usuelle des PID



Définition de la PHS

- Maladie inflammatoire et/ou fibreuse affectant le parenchyme pulmonaire et les petites VA
- Typiquement : réaction immuno-médiée après exposition à un antigène inhalé
- Antigène non identifié dans 30 à 50% des cas …

- Aiguë / Subaiguë / Chronique : termes abandonnés

PHS fibreuse

Ou

PHS non fibreuse

Am J Respir Crit Care Med Vol 202, Iss 3, pp e36–e69, Aug 1, 2020

Epidémiologie des PHS

Table 2. ILD Diagnosis among Patients in ILD-India Registry Cohort

Type of ILD	Number of Patients (%)
Hypersensitivity pneumonitis	513 (47.3)
Connective tissue–associated ILD	151 (13.9)
Idiopathic pulmonary fibrosis	148 (13.7)
Idiopathic nonspecific interstitial pneumonia	92 (8.5)
Sarcoidosis	85 (7.8)
Pneumoconiosis	33 (3.0)

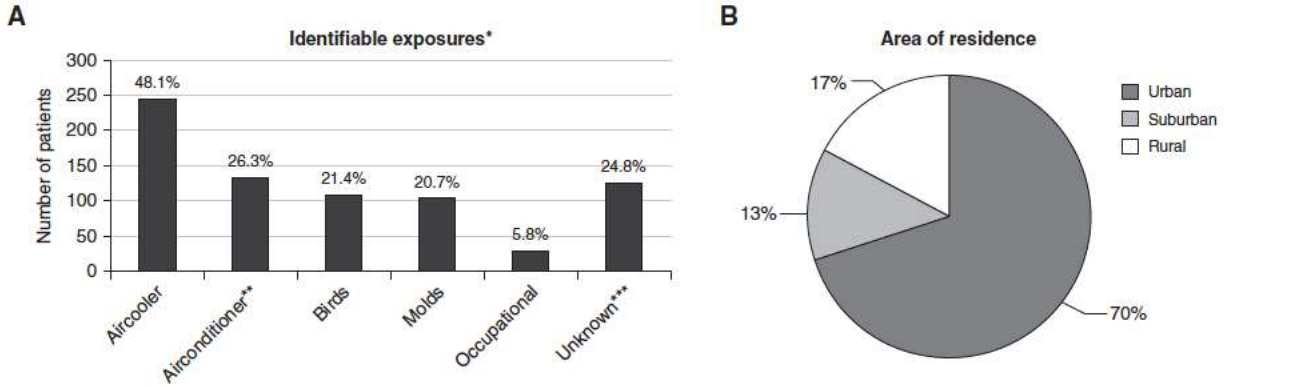
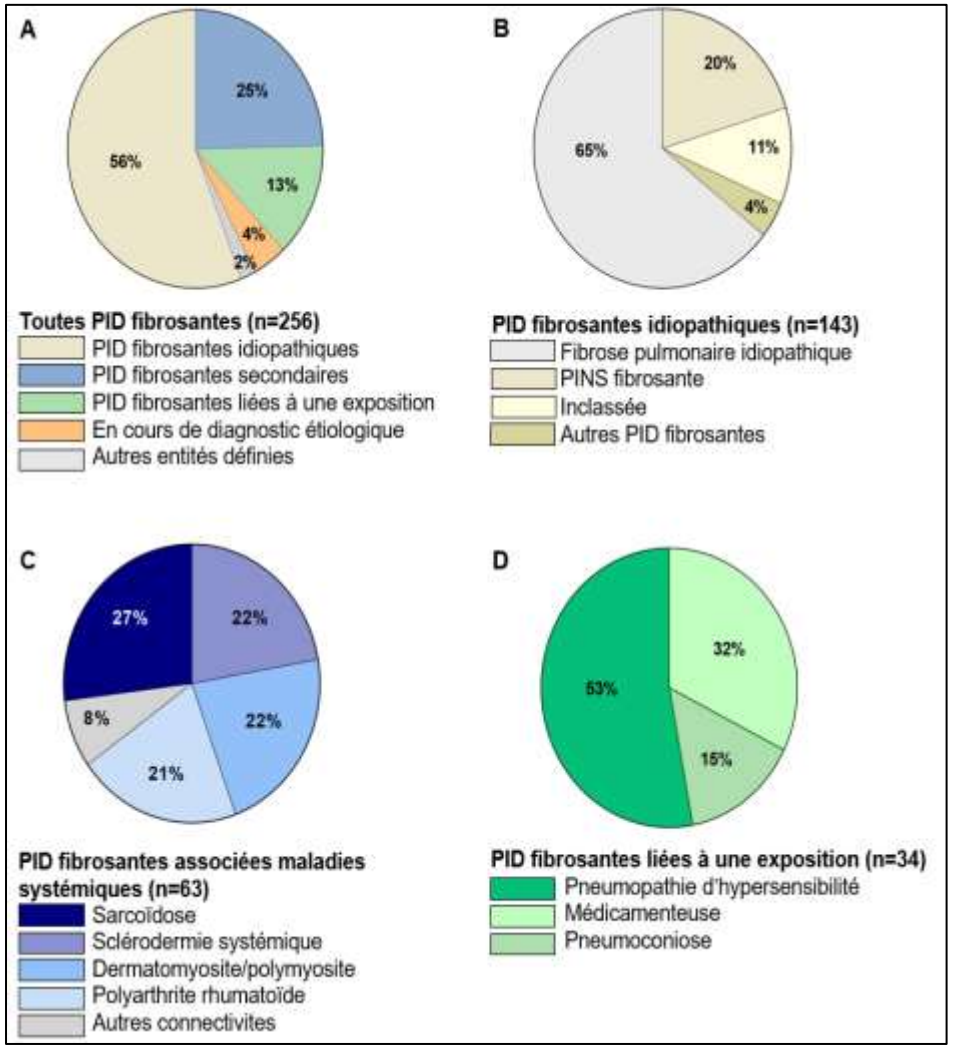


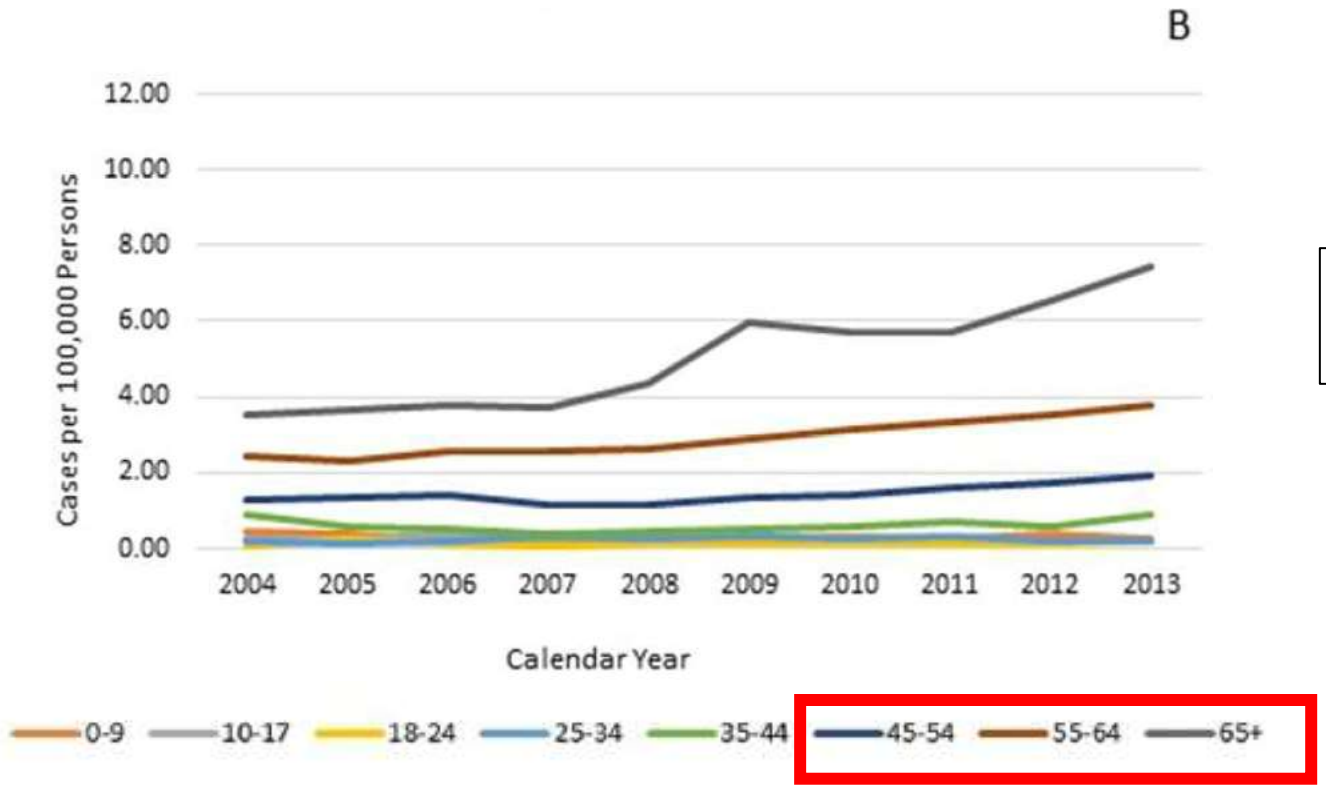
Figure 5. (*A*) Identifiable exposures among 513 patients with hypersensitivity pneumonitis (HP). (*B*) Patients with HP (n = 513) by area of residence. *Numbers do not add to 100% because some patients had multiple exposures. **Although it is unknown if exposure to air conditioners is associated with HP, general practice in India is not to clean air conditioners on a regular basis, so it is conceivable that mold could grow in these units. People with air conditioners may then have occult exposure to mold dispersed into the environment. ***24.8% of patients with HP did not have overt exposures to known causes of HP, which is in keeping with reports of insidious or unknown exposures in the literature (42, 43).

Am J Respir Crit Care Med Vol 195, Iss 6, pp 801–813, Mar 15, 2017



Villeneuve RMR 2021

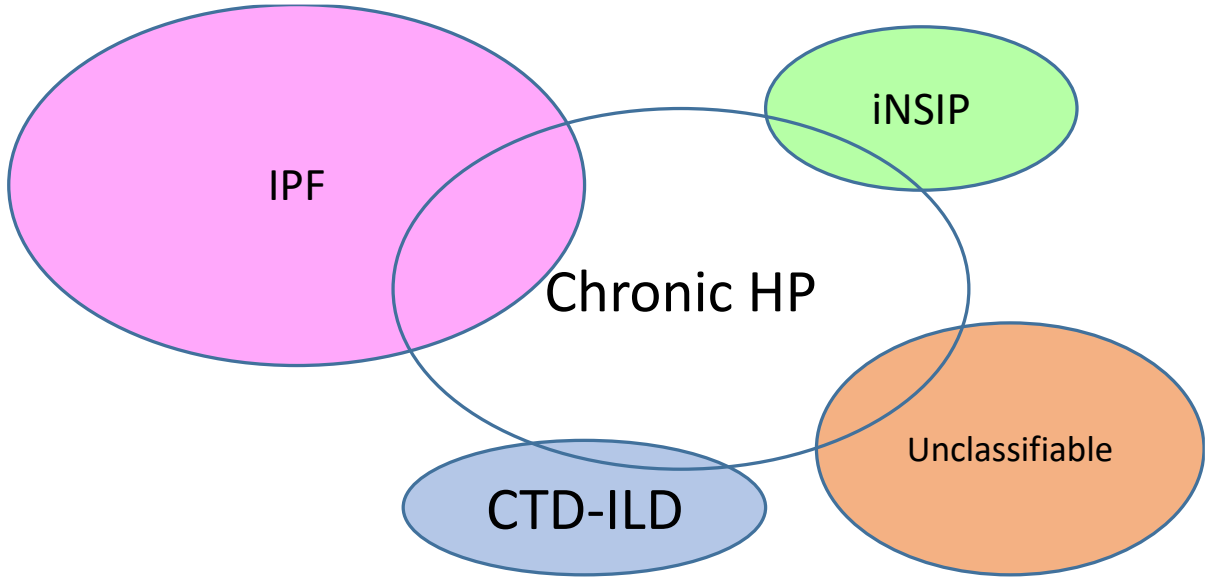
Prevalence of chronic hypersensitivity pneumonitis



Prévalence estimée à 2/100000 hbt aux US

Ann Am Thorac Soc 2018 Apr;15(4):460-469

PHSf : un diagnostic difficile



Chronic hypersensitivity pneumonitis in patients diagnosed with idiopathic pulmonary fibrosis: a prospective case-cohort study

Ferran Morell, Ana Villar, María-Ángeles Montero, Xavier Muñoz, Thomas V Colby, Sudhakar Pipvath, María-Jesús Cruz, Ganesh Raghu

Lancet Respir Med 2013

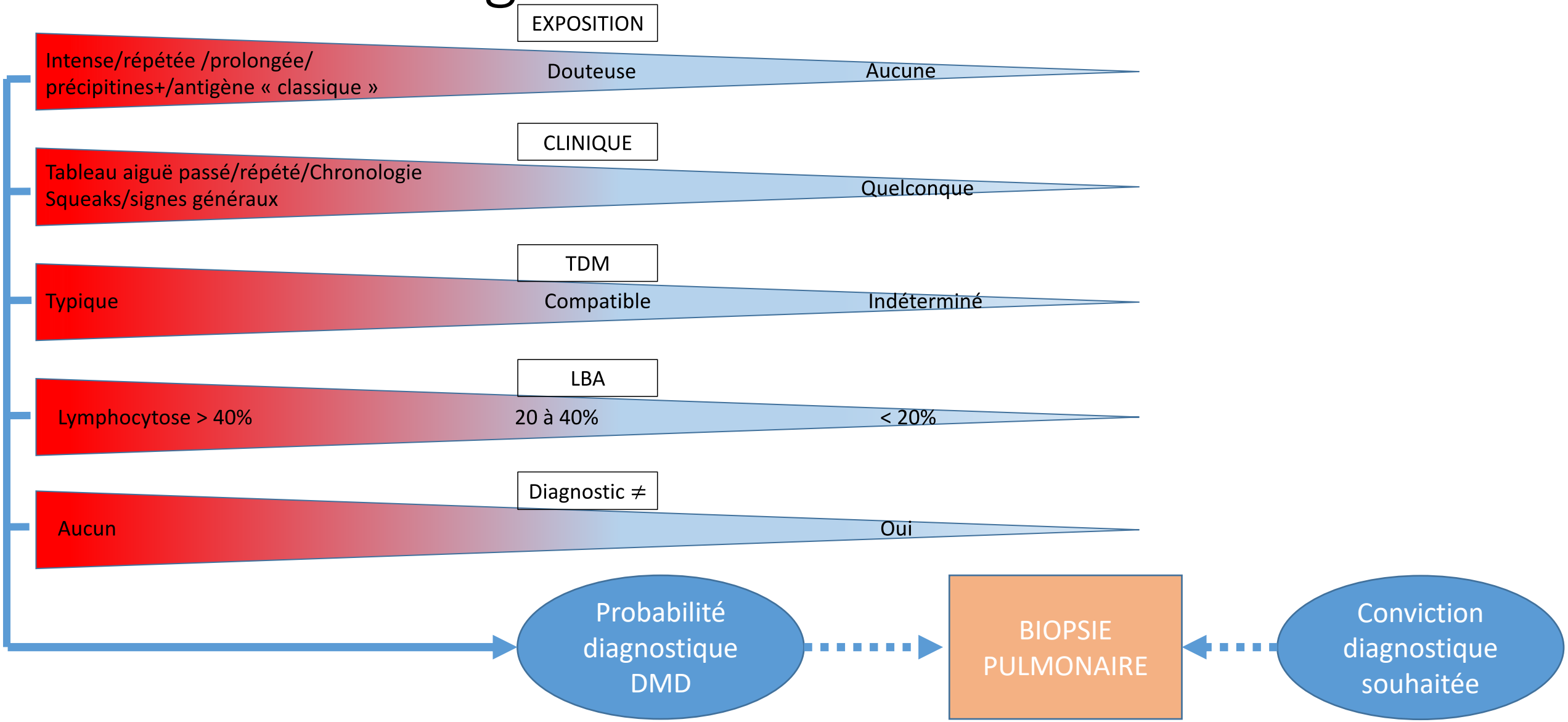
	Clinicians (κw)	Radiologists (κw)	Pathologists (κw)	MDTM (κw)
Idiopathic pulmonary fibrosis	0·72 (0·67–0·76)	0·60 (0·46–0·66)	0·58 (0·45–0·66)	0·71 (0·64–0·77)
Connective tissue disease-related interstitial lung disease	0·76 (0·70–0·78)	0·17 (0·08–0·31)	0·21 (0·06–0·36)	0·73 (0·68–0·78)
Non-specific interstitial pneumonia	0·31 (0·27–0·41)	0·32 (0·26–0·41)	0·30 (0·00–0·53)	0·42 (0·37–0·49)
Hypersensitivity pneumonitis	0·42 (0·30–0·47)	0·35 (0·29–0·43)	0·26 (0·10–0·45)	0·29 (0·24–0·40)

Data are median (IQR). MDTM=multidisciplinary team meeting.

Table 4: **Weighted kappa values (κw) for estimation of diagnostic likelihood for individual diagnoses of diffuse parenchymal lung disease**

Lancet Respir Med 2016

PHSf : un diagnostic difficile



Recherche de la source antigénique

TABLE 3 Evidence-based exposure screening questionnaire

	Number of published cases	Number of publications
1. Have you been exposed to birds or feather/down-containing items?		
☐ YES ☐ NO Bird: Pet birds (tropical), pigeon breeding or other birds in your environment? (duck and geese)	243	26
☐ YES ☐ NO Feather/down-containing items (duck or goose down-containing jackets, pillows, blankets or feather dusters)?	111	7
☐ YES ☐ NO Exposure to bird droppings in a farm, factory, or home setting (droppings in an attic, barn, porch or yard)?	2	1
2. Have you had any of the following in your home or work environment?		
☐ YES ☐ NO Humidifiers or mist fountains	17	5
☐ YES ☐ NO Mould or mildew	13	10
☐ YES ☐ NO Moist or decayed wood	9	6
☐ YES ☐ NO Flood/water damage	4	4
☐ YES ☐ NO Straw mats	2	1
☐ YES ☐ NO Window or single unit air conditioners	1	1
☐ YES ☐ NO Oil fan heater	1	1
☐ YES ☐ NO Steam iron	1	1
3. Do you frequently use a hot tub, jacuzzi or sauna? ☐ YES ☐ NO	58	17
4. Have you had any of the following occupations or hobbies or worked in any of the following locations?		
☐ YES ☐ NO Farm/greenhouse worker	295	20
☐ YES ☐ NO Machine operator	48	5
☐ YES ☐ NO Mushroom worker or worker in mushroom factories	42	8
☐ YES ☐ NO Carpenter/sawmill worker or worked in a hardwood processing plant	16	5
☐ YES ☐ NO Wind or brass musical instrument (e.g. saxophone, bassoon, tenor horn, bagpipe)	5	4
☐ YES ☐ NO Painter or paint sprayer	5	2
☐ YES ☐ NO Garbage collector	5	2
☐ YES ☐ NO Well digger	5	1
☐ YES ☐ NO Baker	3	2
☐ YES ☐ NO Working with plaster	1	1
☐ YES ☐ NO Plastic welder	1	1
☐ YES ☐ NO Food production or processing: salami, dry sausage, green tea, onion, potato, flour, wheat, seafood	17	9
☐ YES ☐ NO Cork factory	17	2
☐ YES ☐ NO Repair garage or aircraft manufacturing	10	4
☐ YES ☐ NO Esparto fibre factory	10	2
☐ YES ☐ NO Cosmetic production	2	1
☐ YES ☐ NO Warehouses	1	1
☐ YES ☐ NO Feeding stores/factory	1	1

ERJ Open Res 2020; 6: 00230-2020

Mold in Foam Pillows and Mattresses

A Novel Cause of Hypersensitivity Pneumonitis

Check for updates

Onofre Moran-Mendoza, MD, PhD; Sharina Aldhaheri, MD; Connor J. A. Black, BSc (Hons); Marie Clements-Baker, MD; Mohamed Khalil, MD; and Alexander Boag, MD

Hypersensitivity pneumonitis (HP) is an inflammatory and/or fibrotic disease affecting the lung parenchyma and small airways. It typically results from an immune-mediated reaction provoked by an overt or occult inhaled antigen in susceptible individuals. The chronic or fibrotic form of HP has a poor prognosis, especially when no inciting antigen is identified, which occurs in up to 60% of cases. We report two cases of HP associated with exposure to mold in foam pillows and a mattress, which has not previously been reported as a risk factor for HP. Given the high prevalence of foam in pillows and mattresses, mold in foam in bedding may explain many HP cases with a previously unrecognized cause. Early identification and avoidance of foam in bedding may prevent HP progression to end-stage pulmonary fibrosis and death.

CHEST 2021; 160(3):e259-e263

PO17-428

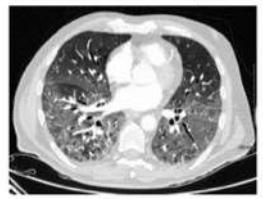
Service de pneumologie

Une pneumonie d'hypersensibilité par ingestat

V Dongay, L Mhanna, G Prévot, E Noël-Savina, M Colombat, L Guilleminault, S Pontier – Marchandise
[1]Toulouse University Hospital - Toulouse (France)

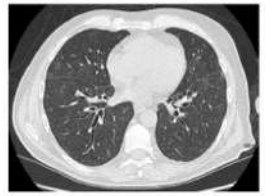
Université Paul Sabatier TOULOUSE III

TDM d'entrée au 2ème épisode

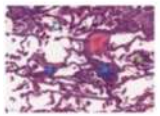


23/04/20

Eviction, antibiothérapie, diurétiques



04/05/20



Le diagnostic de pneumopathie d'hypersensibilité suite à l'ingestion de *Scutallaria Baïcalensis* a été retenu devant :

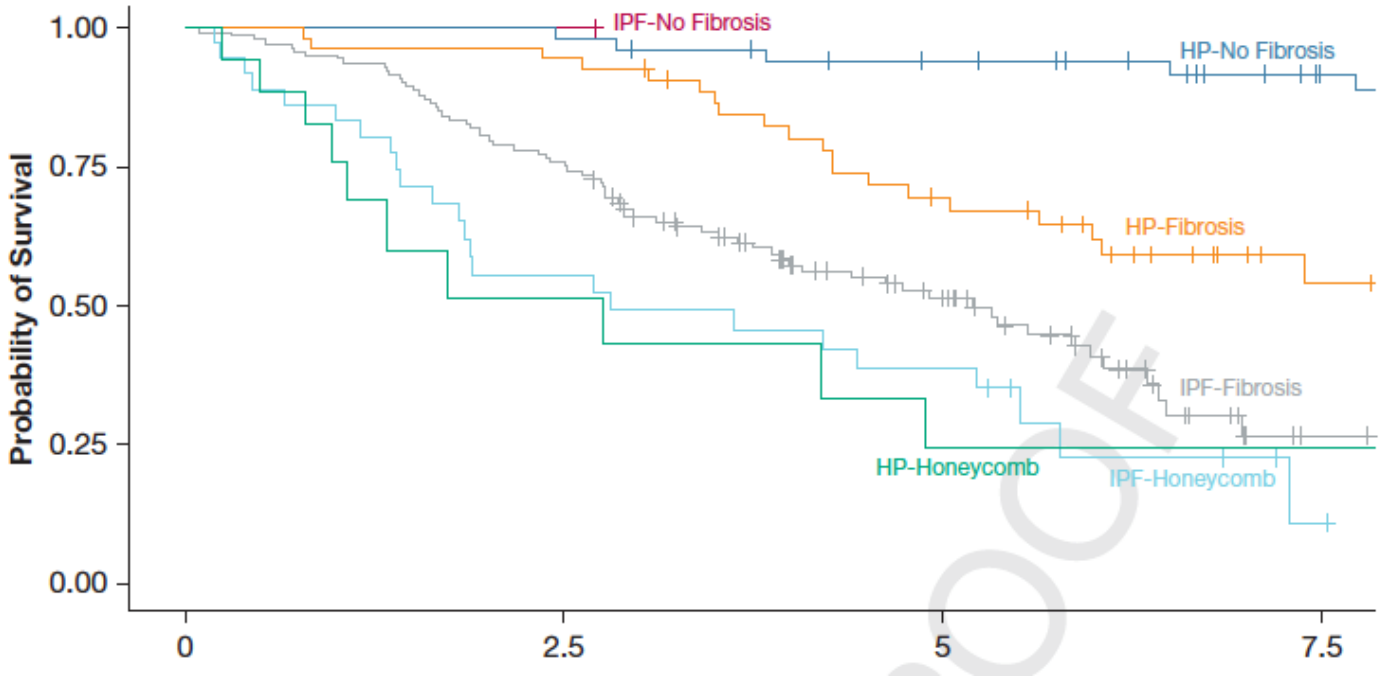
- La biopsie pulmonaire chirurgicale qui suggère un phénomène immuno-allergique sans atteinte bronchiolaire.
- L'absence d'argument pour une participation infectieuse ou cardiogénique.
- Le TDM thoracique retrouvant un aspect non spécifique mais compatible avec une PHS
- Absence de rechute suite à l'arrêt des compléments nutritionnels malgré le retour à domicile

Pronostic de la PHSf

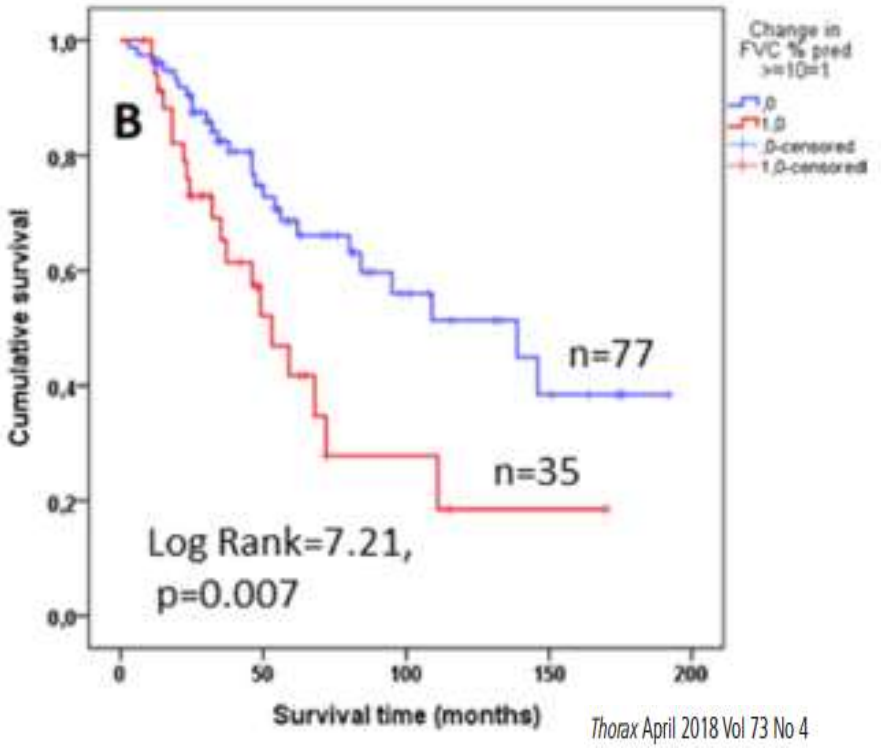
Hypersensitivity Pneumonitis

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

Chest 2019



B). Survival time estimate of chronic hypersensitivity pneumonitis cohort based on decrease <10% (n=77) and ≥10% predicted FVC (n=35) after 6–12-month period of follow-up



Thorax April 2018 Vol 73 No 4

Facteurs pronostics des PHS

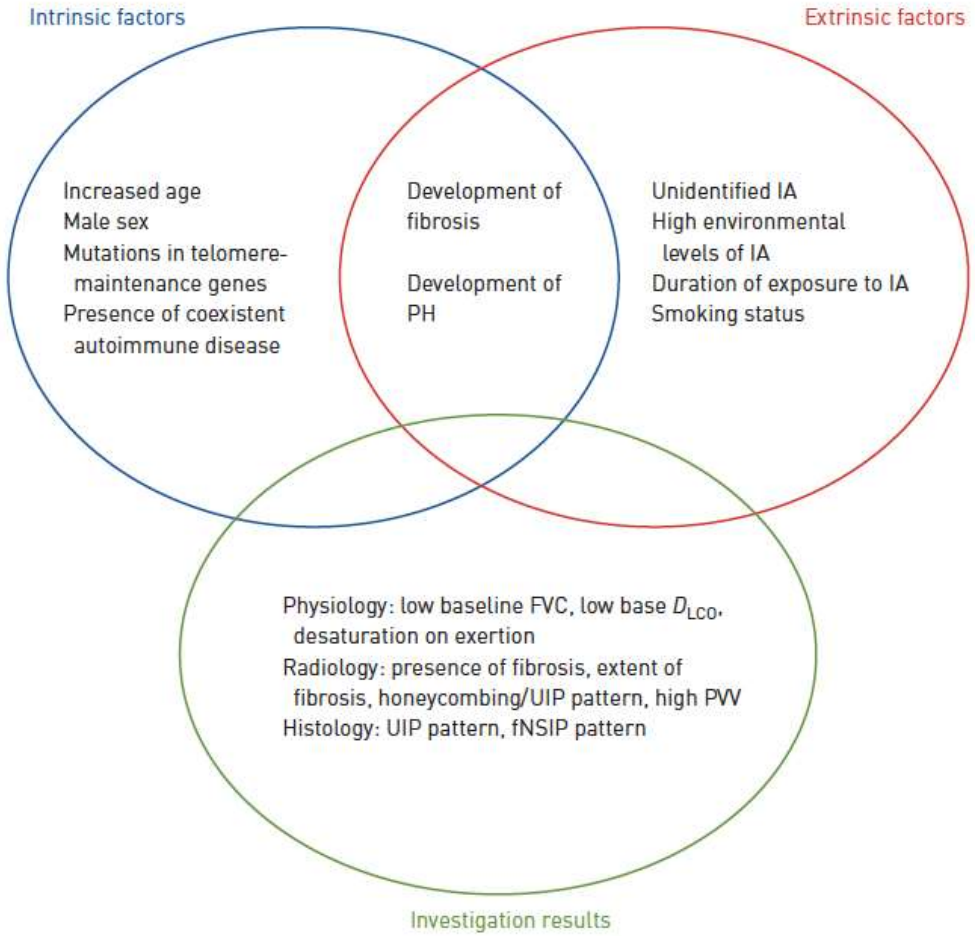


FIGURE 1 Summary of factors associated with increased mortality in hypersensitivity pneumonitis. PH: pulmonary hypertension; IA: inciting antigen; FVC: forced vital capacity; D_{LCO}: diffusing capacity of the lung for carbon monoxide; UIP: usual interstitial pneumonia; PVV: pulmonary vessel volume; fNSIP: fibrotic nonspecific interstitial pneumonia.

Creamer, ERR 2021

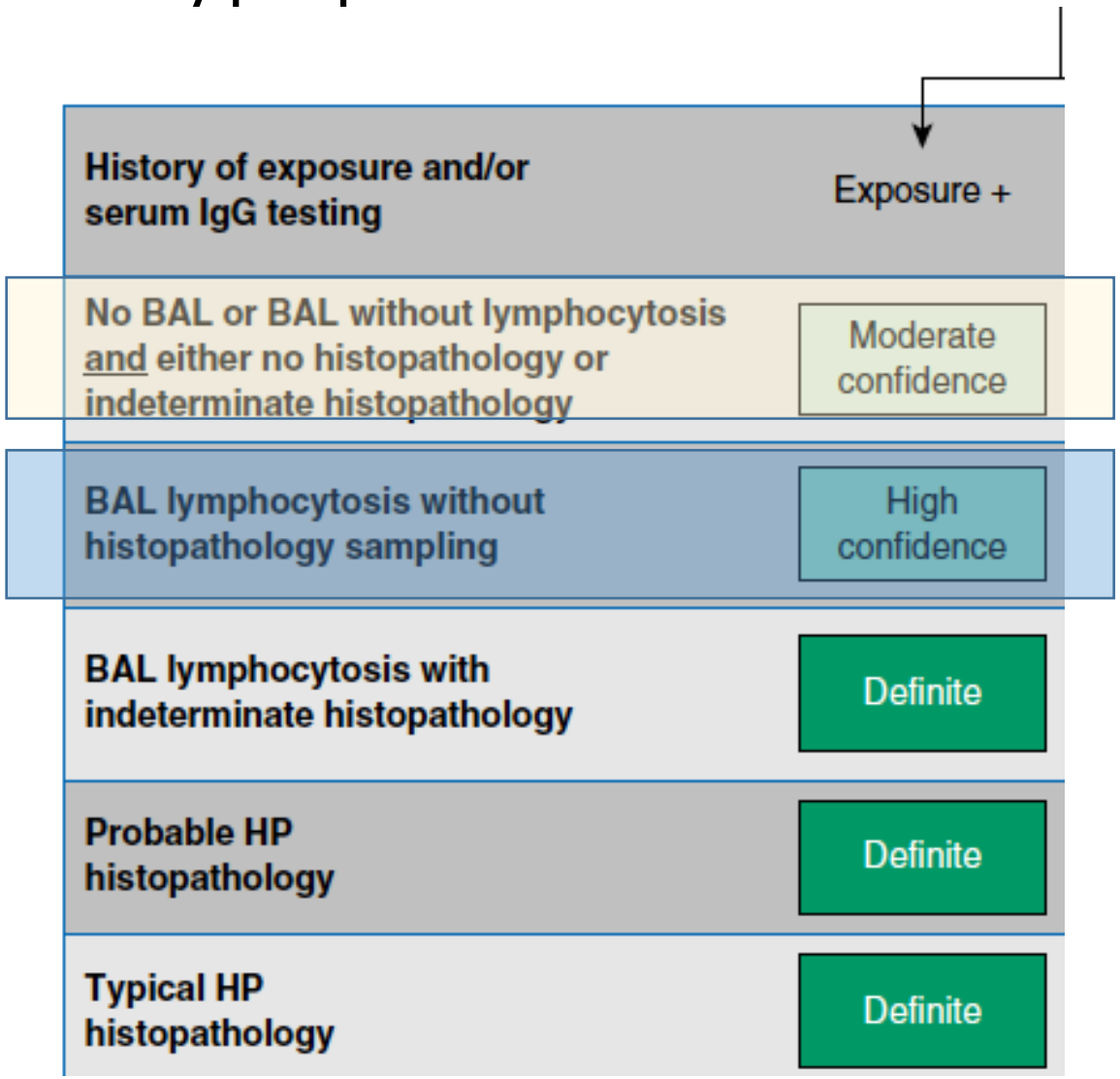
Situation 1 : aspect TDM «typique » de PHSf

- Exposition retrouvée:
  - LBA lymphocytaire

    ⇒certitude diagnostique par BP est certainement futile
  - LBA non lymphocytaire

    ⇒BP peut s'avérer nécessaire

- Definite : >90% confidence
- high-confidence : 80–89%
- moderate-confidence 70–79%
- low-confidence 51–69% diagnoses.



Situation 1 : aspect TDM «typique » de PHSf

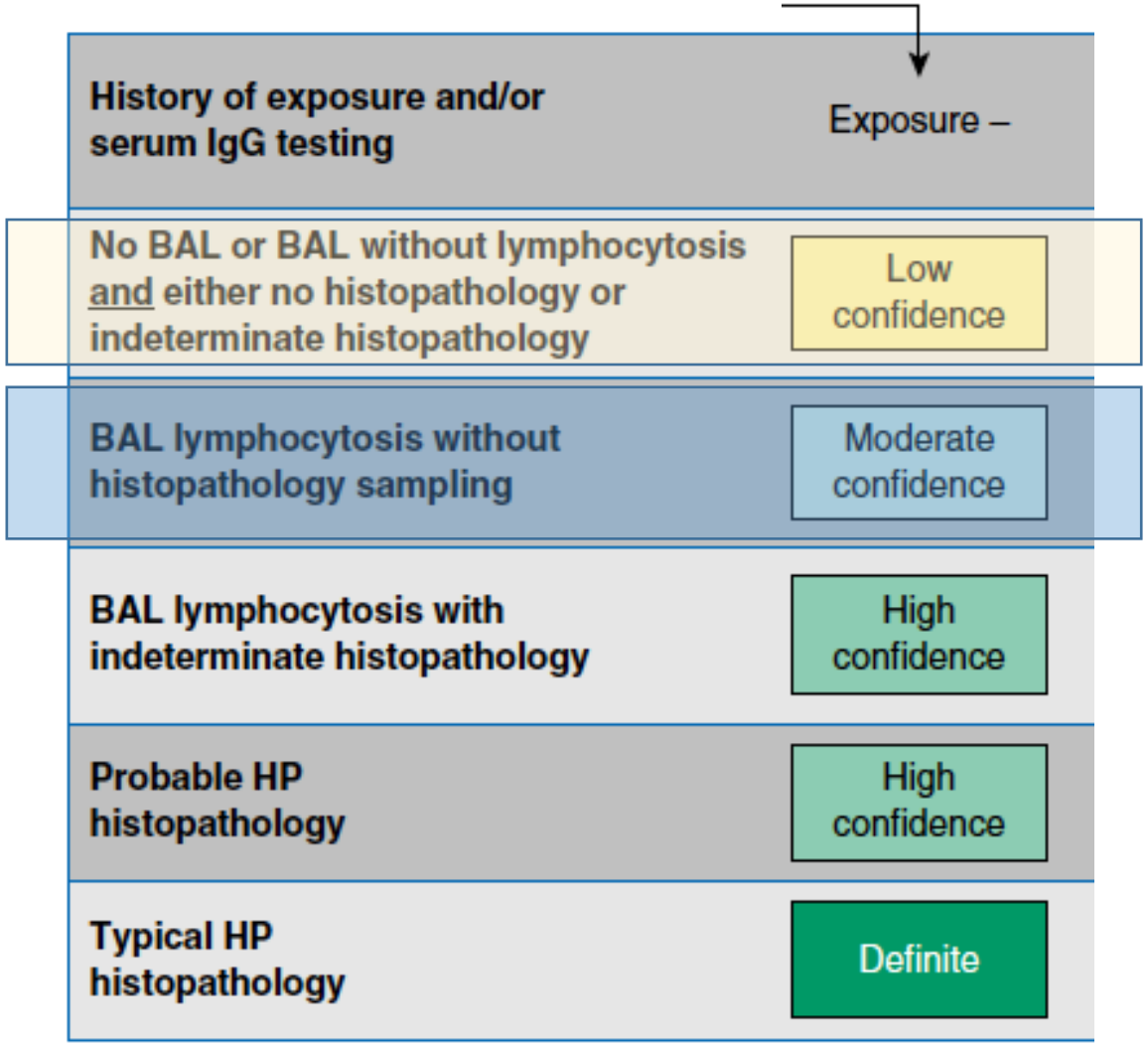
- Exposition non retrouvée:

⇒Un LBA lymphocytaire peut suffire si l'exigence diagnostique est modeste

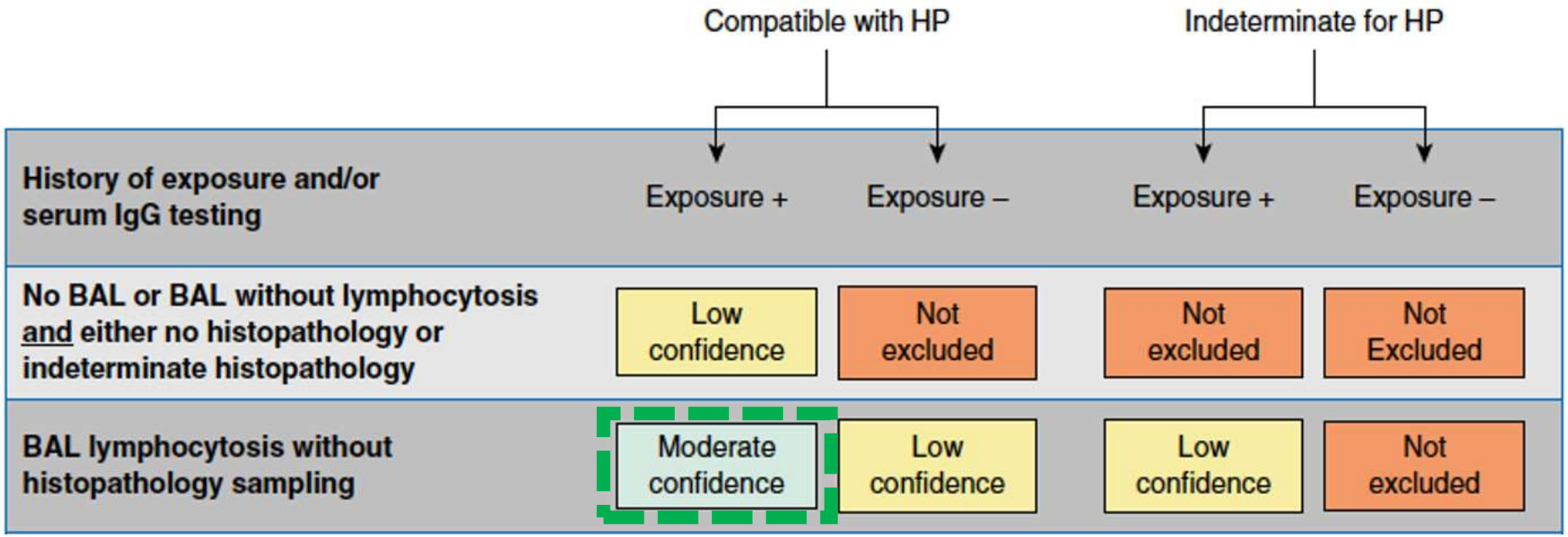
⇒Dans les autres cas, la BP est à envisager si elle est faisable ?

- Rechercher à nouveau l'exposition avant ++

- Definite : >90% confidence
- high-confidence : 80–89%
- moderate-confidence 70–79%
- low-confidence 51–69% diagnoses.



Situation 2 : aspect TDM «compatible» ou « indéterminé » de PHSf



- Definite : >90% confidence
- high-confidence : 80–89%
- moderate-confidence 70–79%
- low-confidence 51–69% diagnoses.

Situation 2 : aspect TDM «compatible» ou « indéterminé » de PHSf

- La BP sera souvent nécessaire

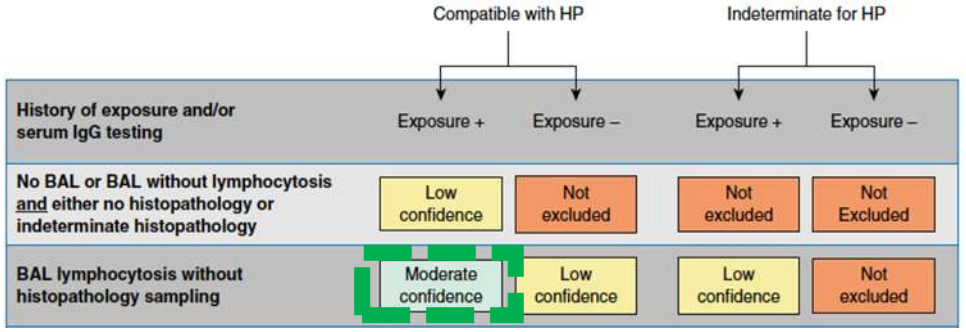
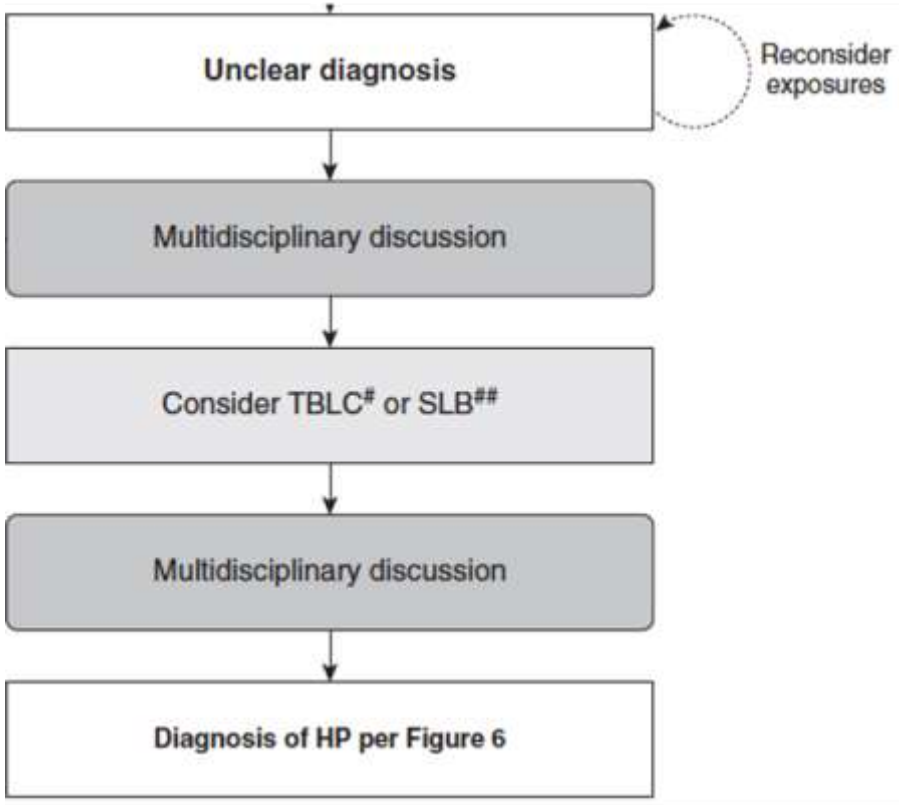


Tableau 5. Principales contre-indications à la biopsie pulmonaire vidéo-chirurgicale

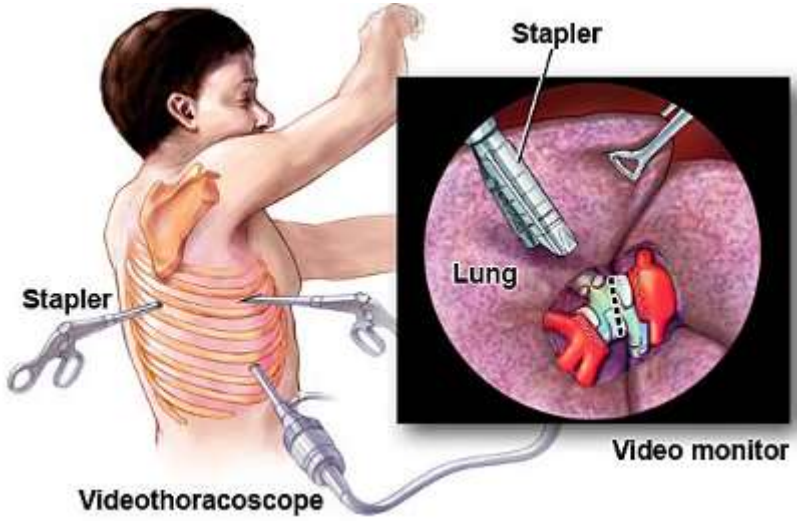
- Âge physiologique > 75 ans
- Aggravation rapide de la maladie
- Faible réserve respiratoire (CVF < 60-70 %, DLco < 35-40 %)
- Oxygénothérapie de longue durée
- Hypertension pulmonaire
- Comorbidités importantes ou multiples
- Immunodépression

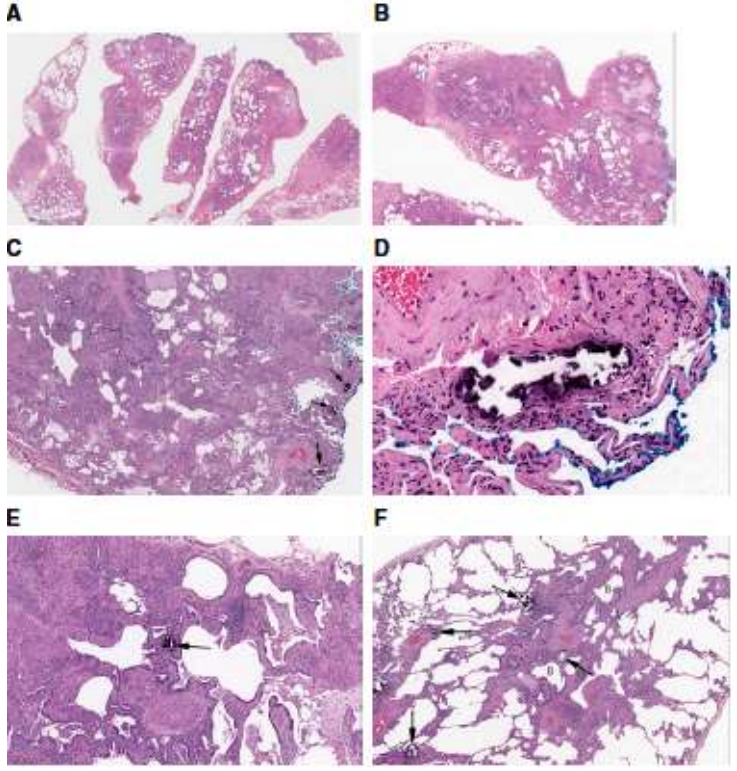


Biopsie Pulmonaire

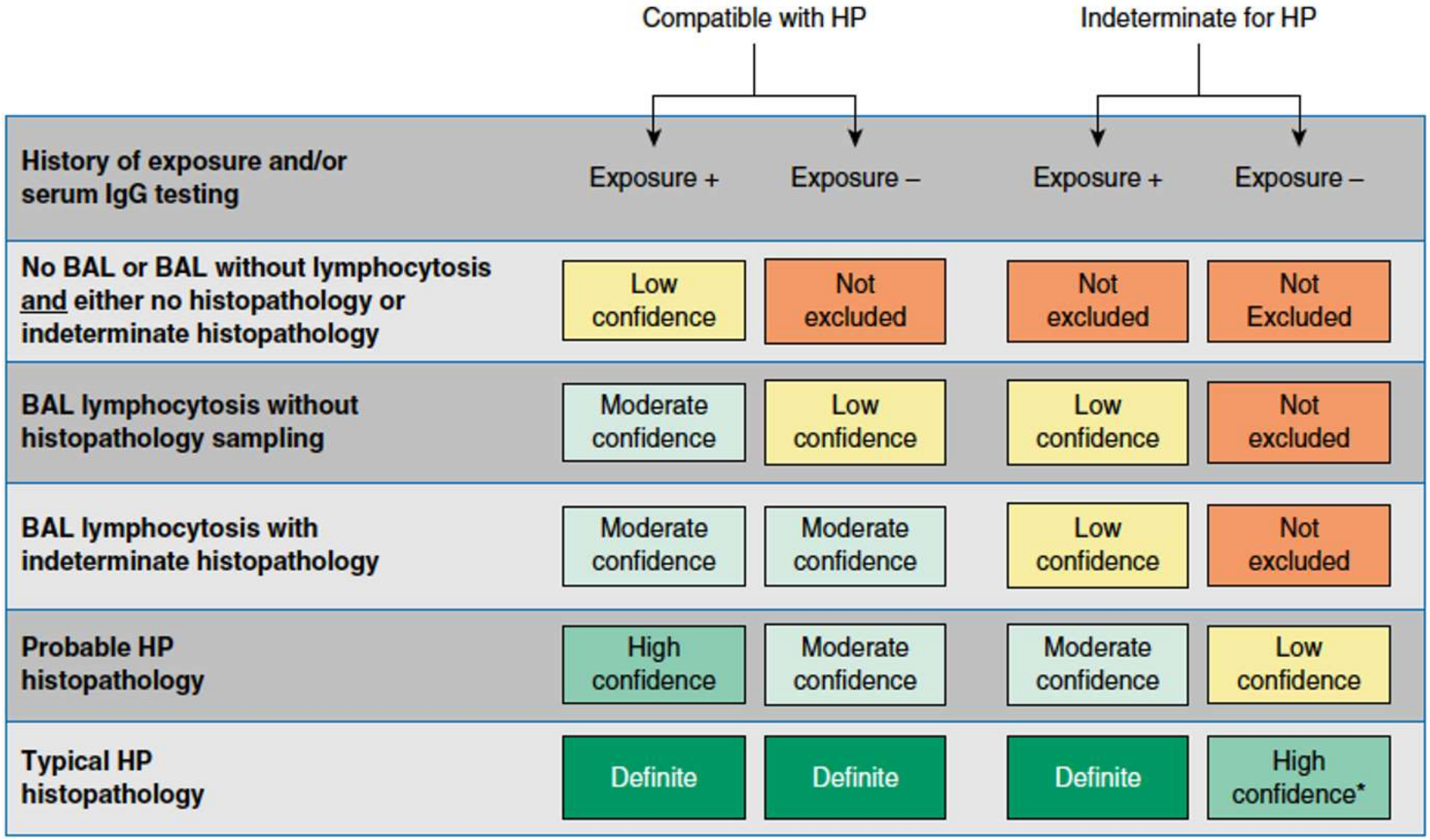
Table 7. Histopathological Criteria for the Diagnosis of HP (Other than "Hot-Tub Lung"*)

HP	Probable HP	Indeterminate for HP
Fibrotic HP‡ Typical histopathological features of fibrotic HP; *1 or 2 and 3* in at least one biopsy site: 1. Chronic fibrosing interstitial pneumonia • Architectural distortion, fibroblast foci ± subpleural honeycombing • Fibrotic NSIP-like§ pattern 2. Airway-centered fibrosis • ±Peribronchiolar metaplasia • ±Bridging fibrosis‖	Both of the following features (*1 or 2* from first column) in at least one biopsy site: 1. Chronic fibrosing interstitial pneumonia • Architectural distortion, fibroblast foci ± subpleural honeycombing • Fibrotic NSIP-like pattern 2. Airway-centered fibrosis • ±Peribronchiolar metaplasia • ±Bridging fibrosis‖ ±Cellular interstitial pneumonia ±Organizing pneumonia pattern ±Cellular bronchiolitis *and* Absence of features in any biopsy site to suggest an alternative diagnosis • Plasma cells > lymphs • Extensive lymphoid hyperplasia • Extensive well-formed sarcoidal granulomas and/or necrotizing granulomas • Aspirated particulates	Either one of the following features in at least one biopsy site: 1. Chronic fibrosing interstitial pneumonia • Architectural distortion, fibroblast foci ± honeycombing • Fibrotic NSIP-like pattern ±Cellular interstitial pneumonia ±Cellular bronchiolitis ±Organizing pneumonia pattern *and* Absence of features in any biopsy site to suggest an alternative diagnosis • Plasma cells > lymphs • Extensive lymphoid hyperplasia • Extensive well-formed sarcoidal granulomas and/or necrotizing granulomas • Aspirated particulates
3. Poorly formed nonnecrotizing granulomas† ±Cellular interstitial pneumonia ±Cellular bronchiolitis ±Organizing pneumonia pattern *and* Absence of features in any biopsy site to suggest an alternative diagnosis • Plasma cells > lymphs • Extensive lymphoid hyperplasia • Extensive well-formed sarcoidal granulomas and/or necrotizing granulomas • Aspirated particulates		





Situation 2 : aspect TDM «compatible» ou « indéterminé » de PHSf : BP effectuée



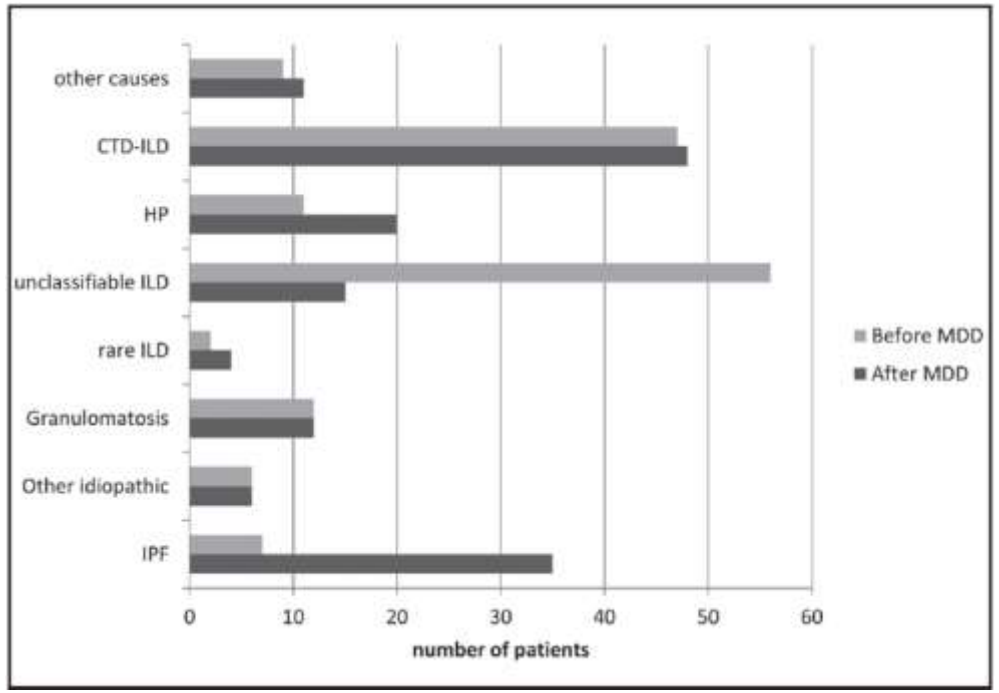
History of exposure and/or serum IgG testing	Compatible with HP: Exposure +	Compatible with HP: Exposure –	Indeterminate for HP: Exposure +	Indeterminate for HP: Exposure –
No BAL or BAL without lymphocytosis and either no histopathology or indeterminate histopathology	Low confidence	Not excluded	Not excluded	Not Excluded
BAL lymphocytosis without histopathology sampling	Moderate confidence	Low confidence	Low confidence	Not excluded
BAL lymphocytosis with indeterminate histopathology	Moderate confidence	Moderate confidence	Low confidence	Not excluded
Probable HP histopathology	High confidence	Moderate confidence	Moderate confidence	Low confidence
Typical HP histopathology	Definite	Definite	Definite	High confidence*

Situation 2 : aspect TDM «compatible» ou « indéterminé » de PHSf : BP non effectuée

MULTIDISCIPLINARY MANAGEMENT OF INTERSTITIAL LUNG DISEASES: A REAL-LIFE STUDY

Caroline Biglia[1], Benoit Ghaye[2], Gregory Reychler[1,2], Sandra Koenig[1], Halil Yildiz[3], Valérie Lacroix[4], Farah Tamirou[5], Delphine Hoton[6], Thierry Pieters[1], Antoine Froidure[1,2]

Sarcoidosis Vasc Diffuse Lung Dis 2019; 36 (2): 108-115



Unclassifiable interstitial lung disease: from phenotyping to possible treatments

Sabina A. Guler[a,b,c] and Christopher J. Ryerson[a,b]

Curr Opin Pulm Med 2018, 24:461–468

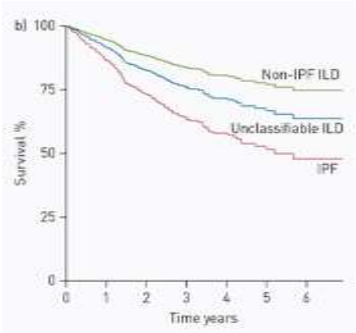
Table 1. Reasons for unclassifiable interstitial lung disease

	Clinical [11,12▪]	Radiological [19▪]	Pathological [20▪]	Multidisciplinary discussion [11,12▪,21]
Incomplete evaluation	Unable to obtain adequate history (e.g., exposures)	Not available	No biopsy performed (e.g., unfavorable risk–benefit ratio, patient preference)	Not available
		HRCT quality insufficient	Insufficient biopsy quality (too small, damaged, nonoptimal sampling location)	Difficult interpretation of poor quality diagnostic material
Overlapping findings	Multiple risk factors predisposing for different specific ILDs	Overlap with non-ILD features (e.g., cardiac failure, infection)	Overlapping histological features	Discrepant clinical, radiological, and pathological features
		Acute exacerbation		Discrepant interpretation of information by members
		Features of different specific ILDs		
Nonspecific findings	Stable disease, mild symptoms	Indeterminate for UIP	Only advanced interstitial fibrosis	Poorly classifiable findings
		Prior treatment (e.g., corticosteroids)	Prior treatment (e.g., corticosteroids)	

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]

Eur Respir J 2013; 42: 750–757 | DOI: 10.1183/09031936.00131912



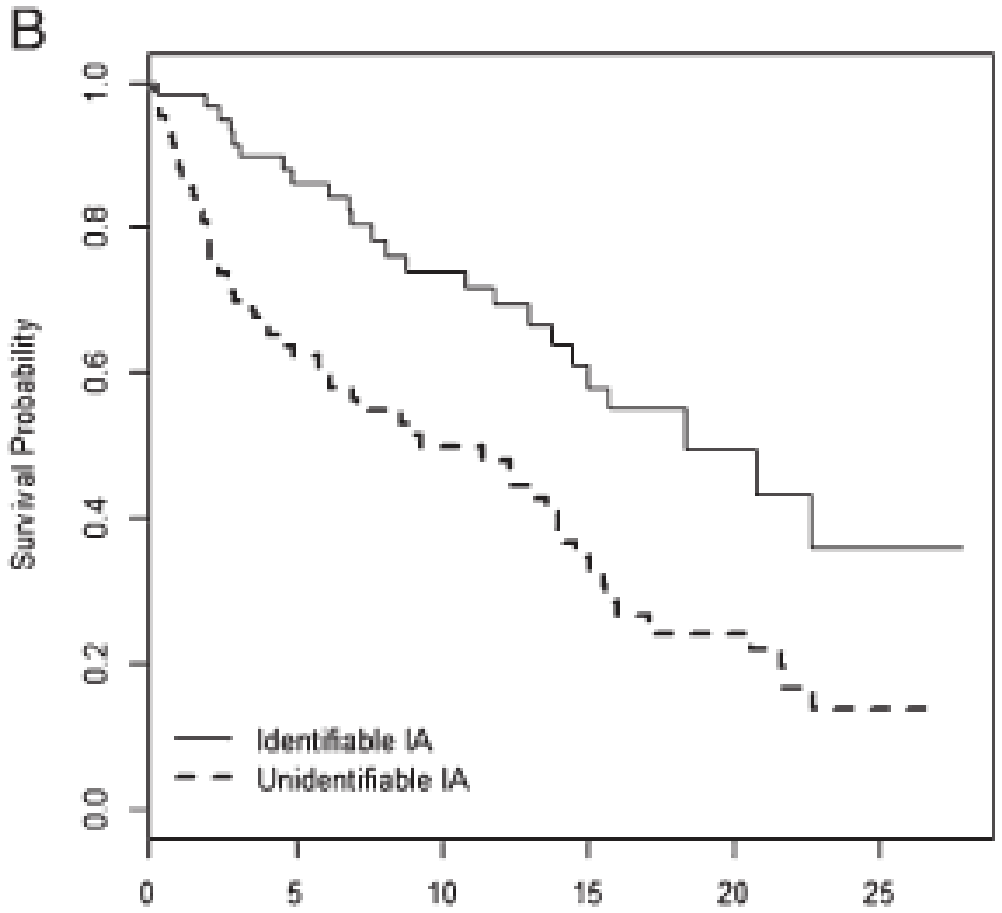
Prise en charge

1- Trouver l'antigène et l'évincer

Identifying an Inciting Antigen Is Associated With Improved Survival in Patients With Chronic Hypersensitivity Pneumonitis

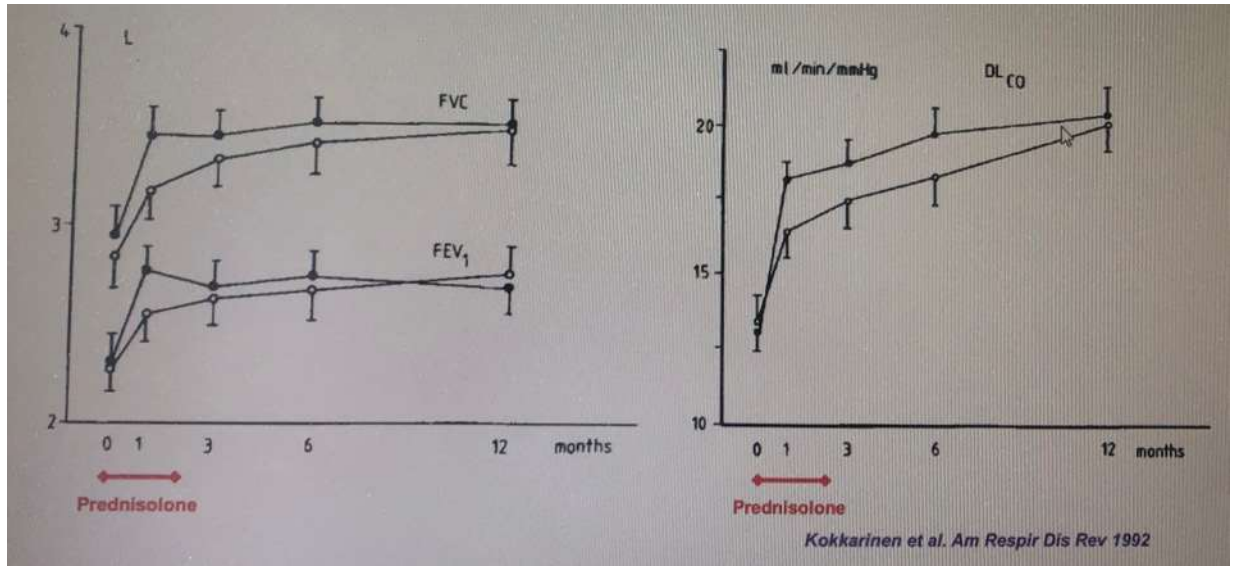
Evans R. Fernández Pérez, MD, FCCP; Jeffrey J. Swigris, DO, FCCP; Anna V. Forssén, MS; Olga Tourin, MD; Joshua J. Solomon, MD, FCCP; Tristan J. Huie, MD, FCCP; Amy L. Olson, MD, MSPH; and Kevin K. Brown, MD, FCCP

CHEST 2013; 144(5):1644–1651



Prise en charge

2- Traiter par corticothérapie



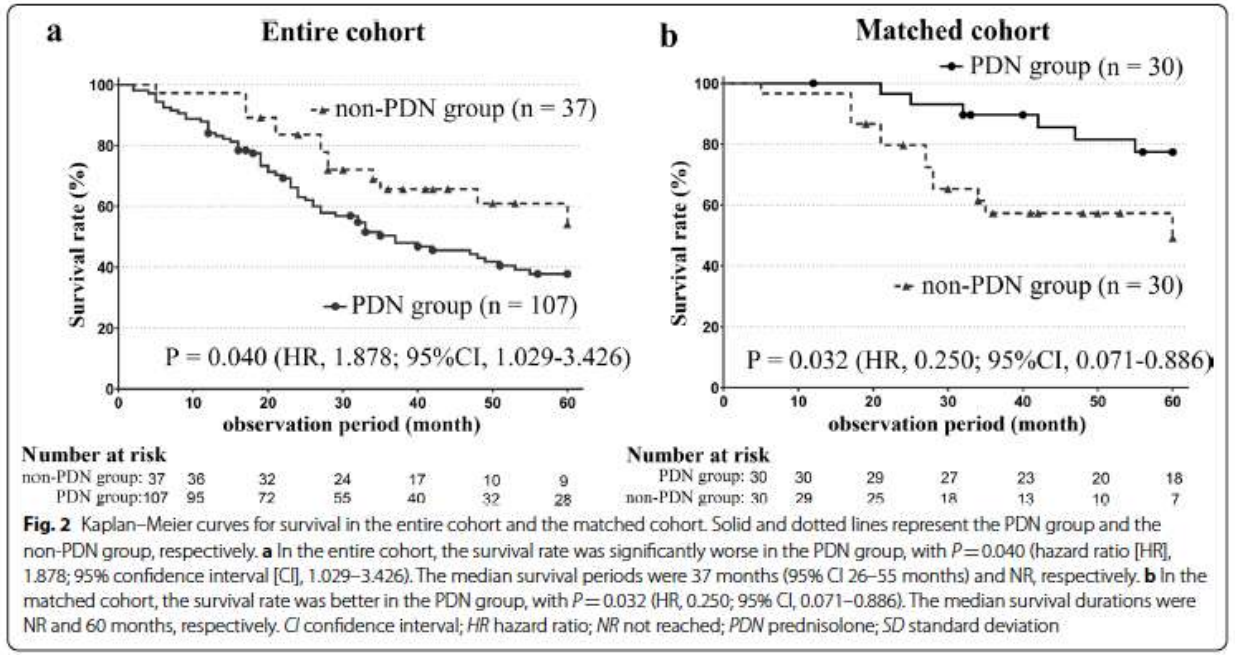


Fig. 2 Kaplan–Meier curves for survival in the entire cohort and the matched cohort. Solid and dotted lines represent the PDN group and the non-PDN group, respectively. **a** In the entire cohort, the survival rate was significantly worse in the PDN group, with $P = 0.040$ (hazard ratio [HR], 1.878; 95% confidence interval [CI], 1.029–3.426). The median survival periods were 37 months (95% CI 26–55 months) and NR, respectively. **b** In the matched cohort, the survival rate was better in the PDN group, with $P = 0.032$ (HR, 0.250; 95% CI, 0.071–0.886). The median survival durations were NR and 60 months, respectively. *CI* confidence interval; *HR* hazard ratio; *NR* not reached; *PDN* prednisolone; *SD* standard deviation

Ejima *et al. BMC Pulm Med* (2021) 21:243

Prise en charge

3- Ajouter des IS ?

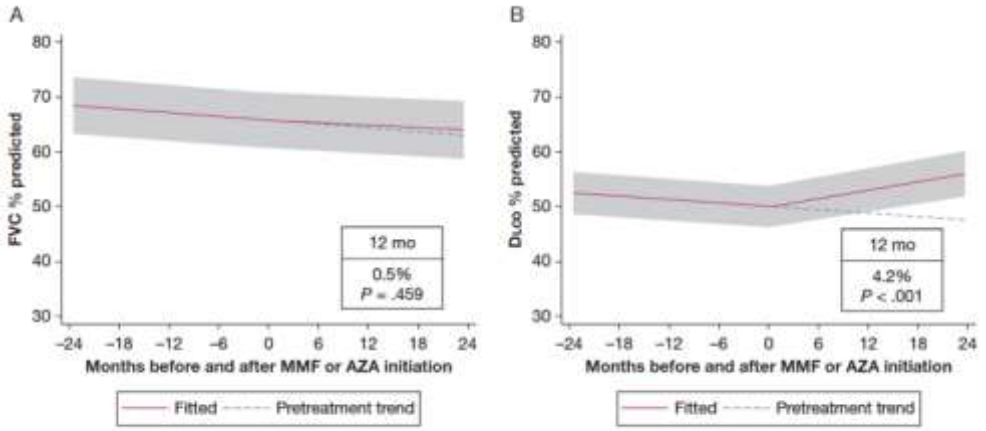
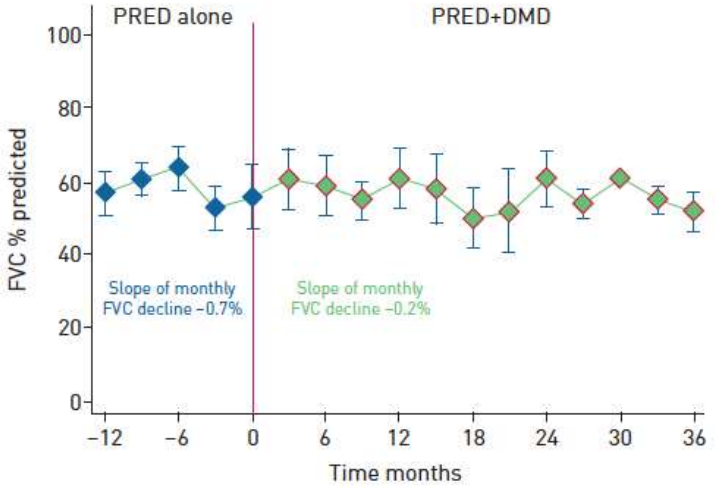
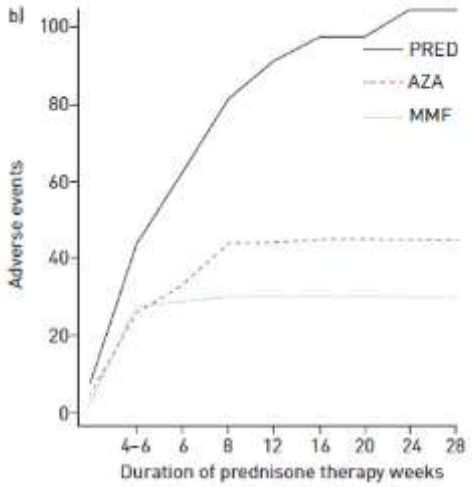


Figure 2 – Mixed-effects model estimates for FVC % predicted and DLCO % predicted before and after initiation of mycophenolate or azathioprine. The gray shading indicates the 95% CI. DLCO = diffusion capacity of the lung for carbon monoxide. See Figure 1 legend for expansion of other abbreviations.

CHEST 2017; 151(3):619-625





ERJ Open Res 2017; 3: 00016-2017

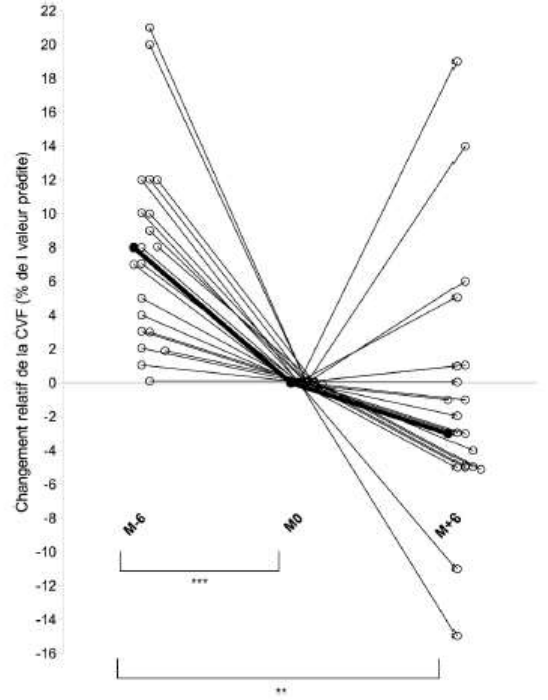


Fig. 1. Relative change in FVC (% of predicted value), 6 months before and after the introduction of rituximab (n = 20The median value is represented by the bold line. ** and ***: p < 0.01 and < 0.001, respectively.

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Traitement des Fibroses Pulmonaires hors FPI

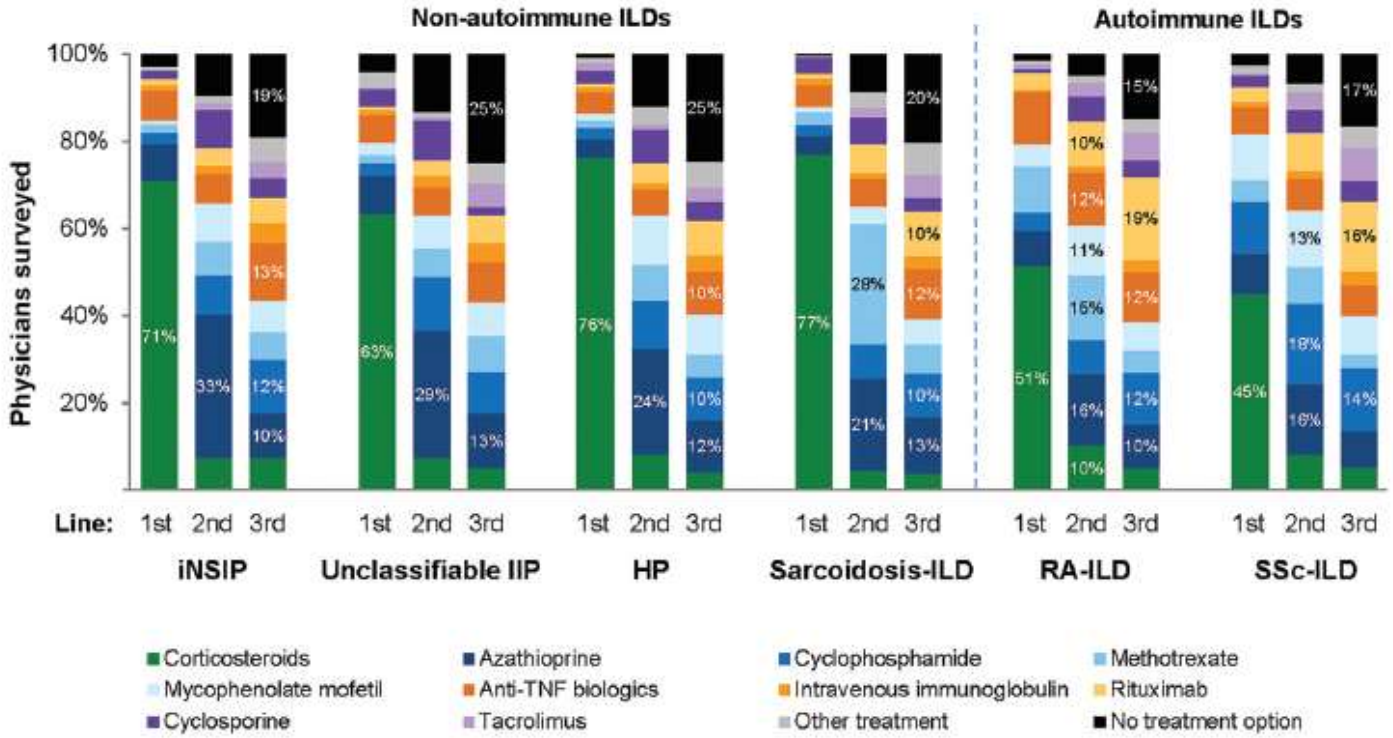


Figure 7. Agents used as first-, second- and third-line treatments for fibrotic ILDs. Data from online survey of physicians (non-autoimmune ILDs: 243 pulmonologists; autoimmune ILDs: 243 pulmonologists and 203 rheumatologists). Survey question: "For the following types of ILDs where patients also have lung fibrosis, please indicate your preferred first, second, and third line treatments for the respective ILD". Rheumatologists were only asked this question in relation to RA-ILD and SSc-ILD. Abbreviations. HP, Hypersensitivity pneumonitis; IIP, Idiopathic interstitial pneumonias; ILD, Interstitial lung disease; iNSIP, Idiopathic non-specific interstitial pneumonia; RA, Rheumatoid arthritis; SSc, Systemic sclerosis.

Wisjenbeek CRMO 2019

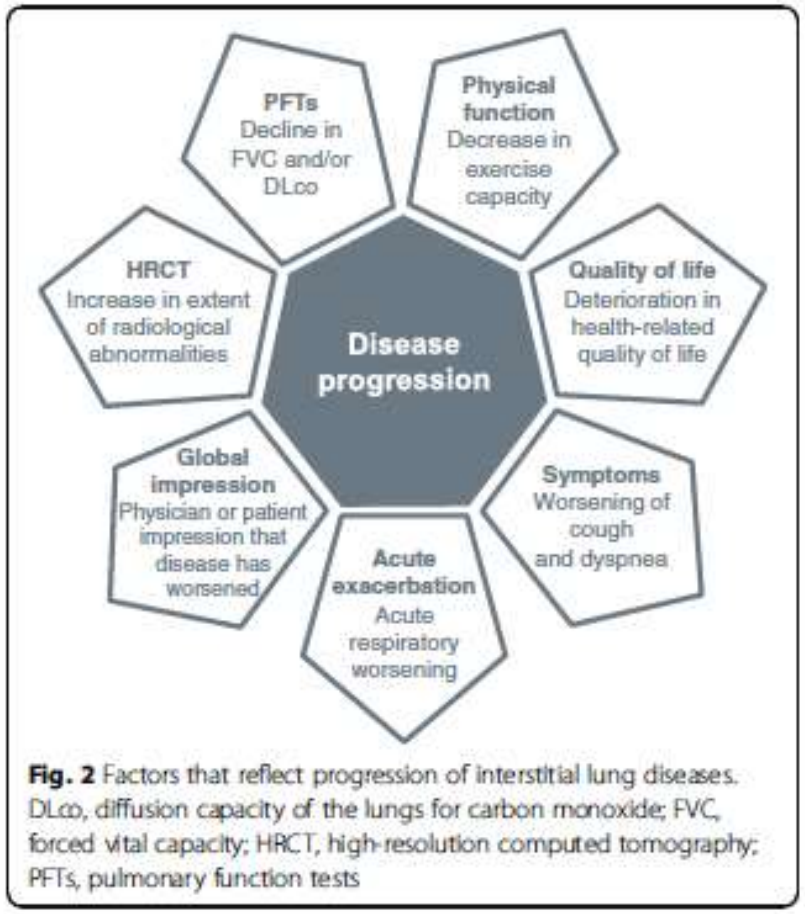
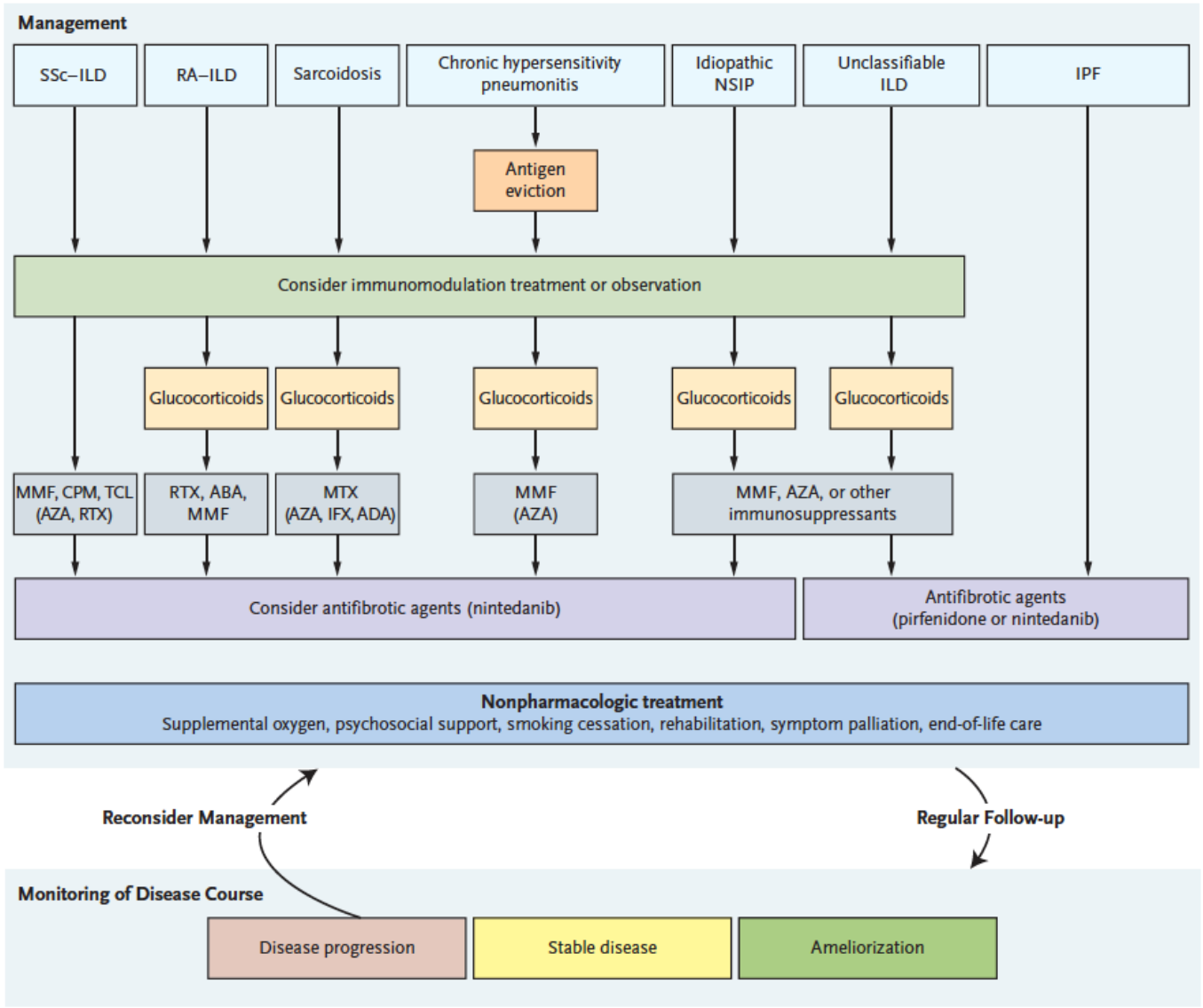


Fig. 2 Factors that reflect progression of interstitial lung diseases. DLco, diffusion capacity of the lungs for carbon monoxide; FVC, forced vital capacity; HRCT, high-resolution computed tomography; PFTs, pulmonary function tests

Kolb Respir Res 2019



Étude INBUILD

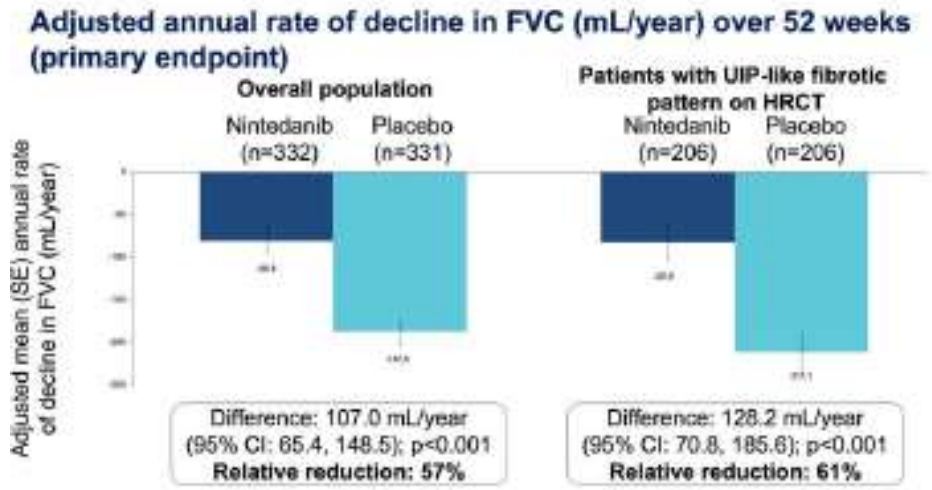
Key inclusion criteria

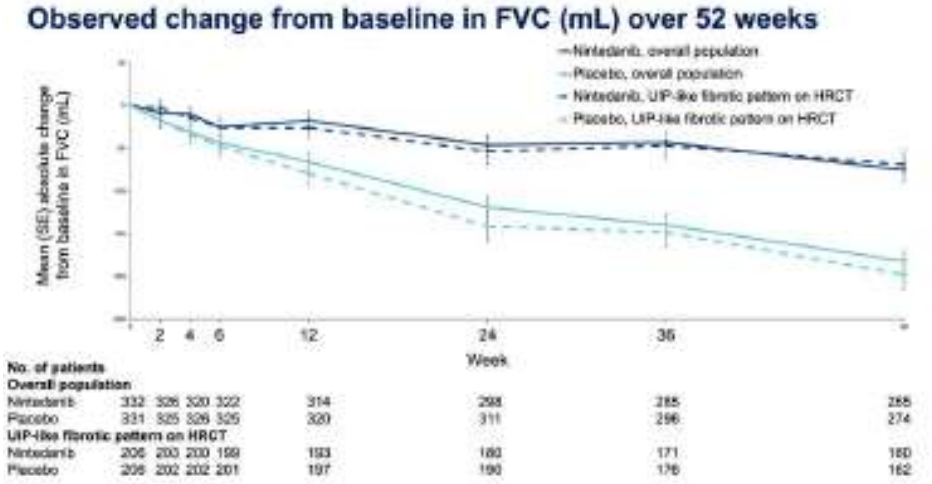
- Physician-diagnosed ILD other than IPF
- Features of diffuse fibrosing lung disease of >10% extent on HRCT performed ≤12 months prior to screening, confirmed by central review
- FVC ≥45% predicted
- DLco ≥30%–<80% predicted

- Progressive phenotype
  - Patients were required to meet ≥1 of the following criteria for ILD progression in the 24 months before screening, despite management:
    - Relative **decline** in **FVC ≥10%** predicted
    - Relative **decline** in **FVC ≥5–<10%** predicted **AND** **Worsened** respiratory **symptoms***
    - Relative **decline** in **FVC ≥5–<10%** predicted **AND** **Increased** extent of **fibrosis on HRCT****
    - **Worsened** respiratory **symptoms*** **AND** **Increased** extent of **fibrosis on HRCT****

Critères de PID fibrosante

FIBROSING LUNG DISEASE ON HRCT *Disease extent of* **>10%**		• Reticular abnormality + Traction bronchiectasis • ± Honeycombing
	Co-existing features allowed	• Ground glass opacity • Upper lung or peribronchovascular predominance • Mosaic attenuation • Air trapping • Centrilobular nodules
	Not allowed	• Widespread consolidation • Progressive massive fibrosis





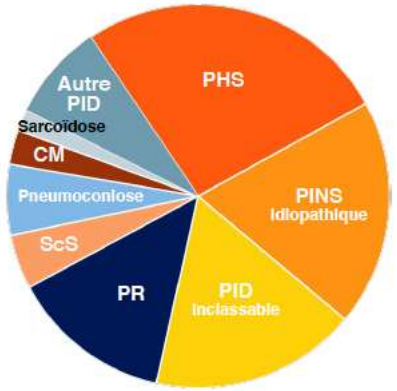
Étude INBUILD

INBUILD Étiologies de la PID à l'inclusion

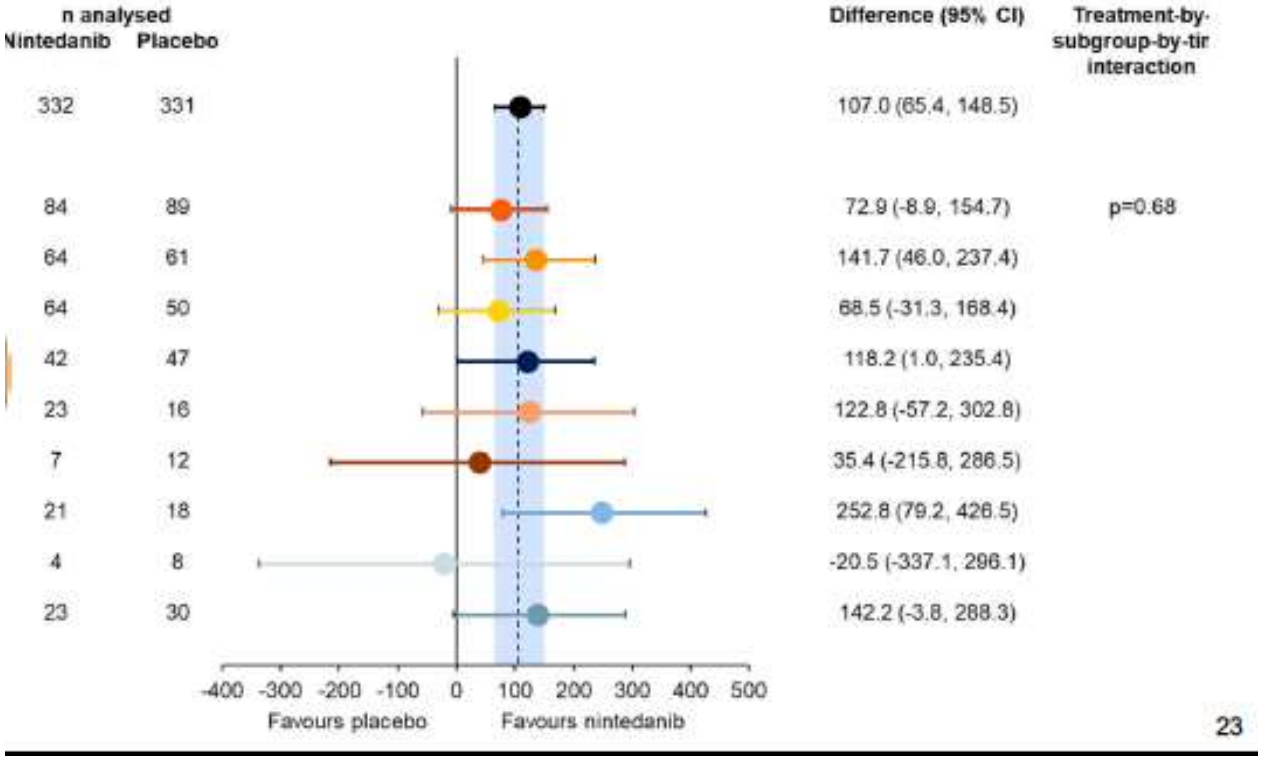
Nintedanib in patients with progressive fibrosing interstitial lung diseases—subgroup analyses by interstitial lung disease diagnosis in the INBUILD trial: a randomised, double-blind, placebo-controlled, parallel-group trial

Lancet Respir Med 2020
Published Online
March 5, 2020

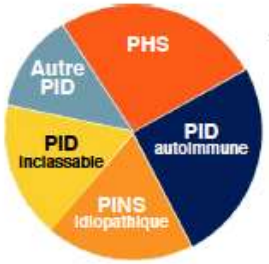
Population INBUILD	
PID autoimmune	25%
Associée à une PR	13% (n=42/47)
Associée à une ScS	6% (n=23/16)
Associée à une CTD mixte	3% (n=7/12)
Autre PID autoimmune	3% (n=10/13)
Sarcoïdose	2% (n=4/8)
PHS	28% (n=84/89)
Pneumoconiose	6% (n=21/18)
PINS idiopathique	19% (n=64/61)
PID inclassable	17% (n=64/50)
Autre PID fibrosante	5% (n=13/17)

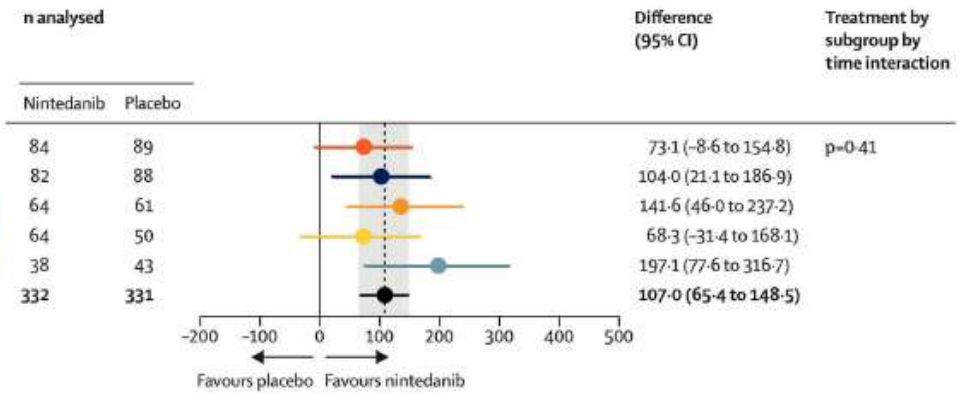


- Wells AU, *et al*. Nintedanib in patients with progressive fibrosing interstitial lung diseases—subgroup analyses by interstitial lung disease diagnosis in the INBUILD trial: a randomised, double-blind, placebo-controlled, parallel-group trial. Lancet Respir Med 2020. [Epub ahead of print]



Taux annuel de déclin de la CVF (mL / an)





Management of Fibrotic Hypersensitivity Pneumonitis

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Clin Chest Med 42 (2021) 311–319