# “Interstitial lung abnormalities (ILA)“

*Quoi en faire en pratique?*

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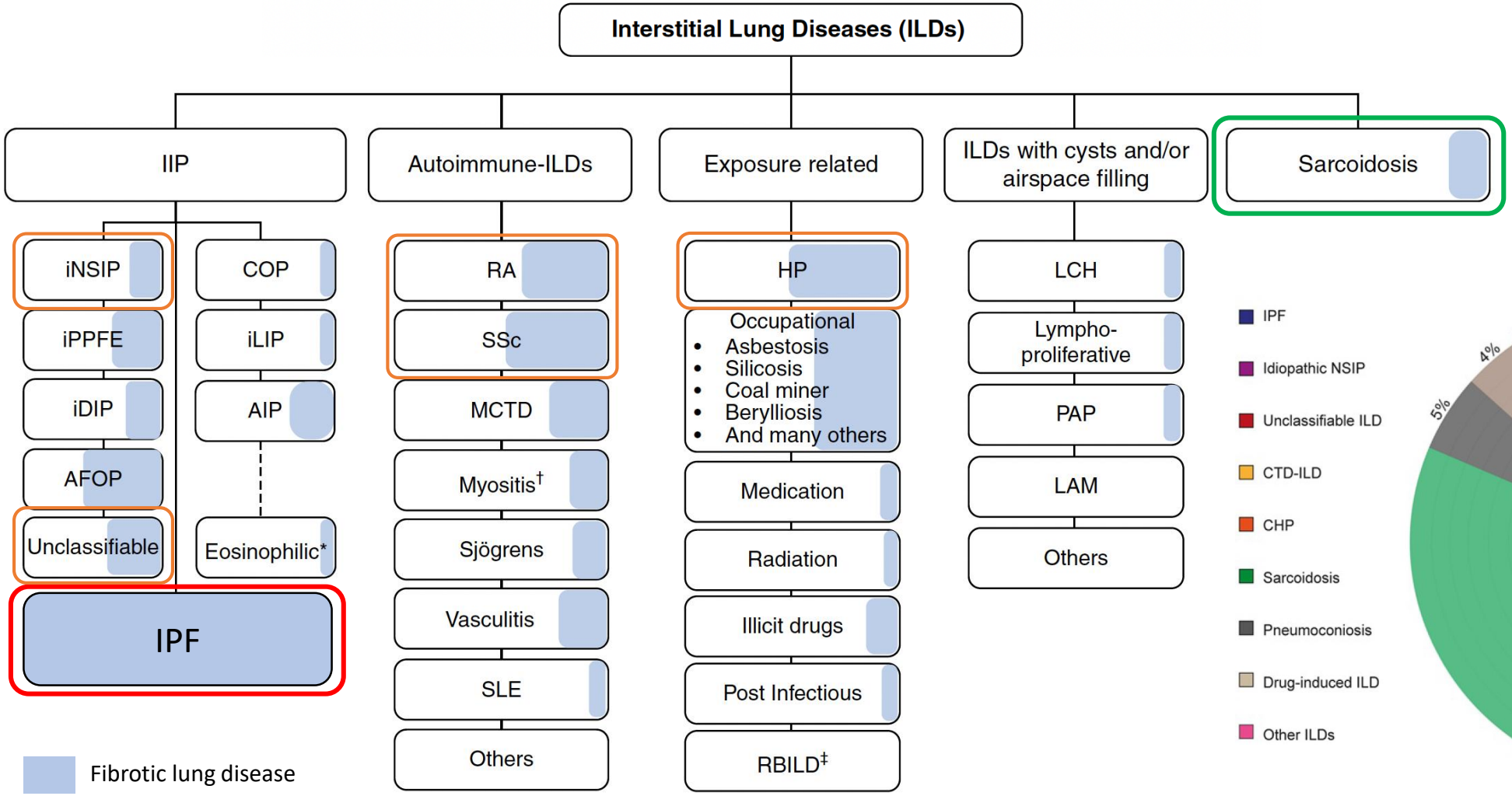
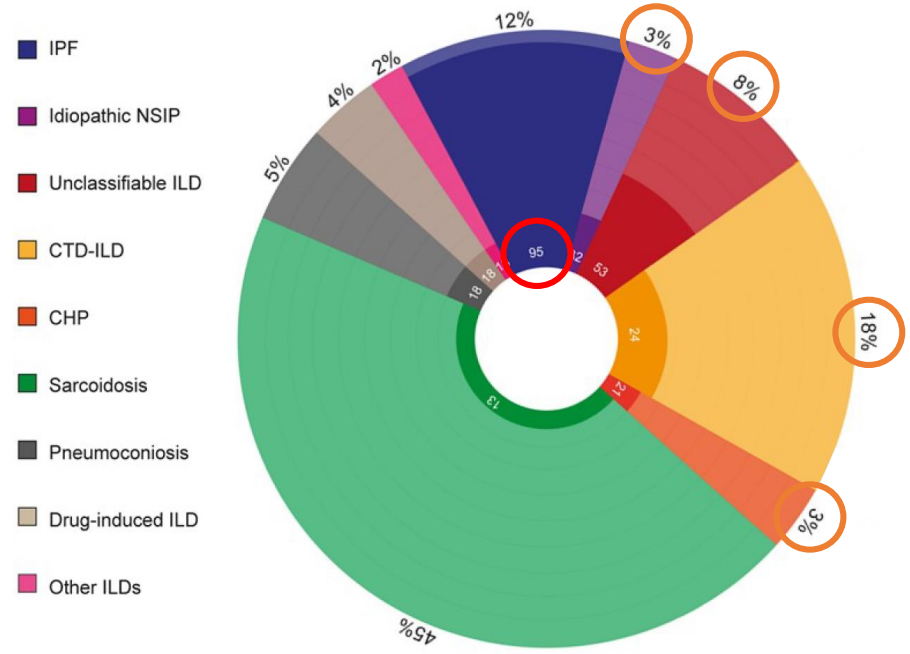
GRC-04 Theranoscan

Pas de lien d’intérêt en relation avec la présentation

# Classification des pneumopathies interstitielles diffuses (PID)

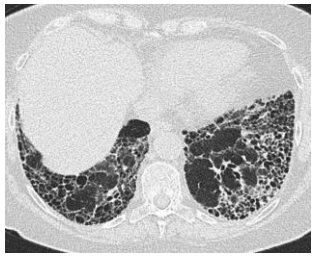


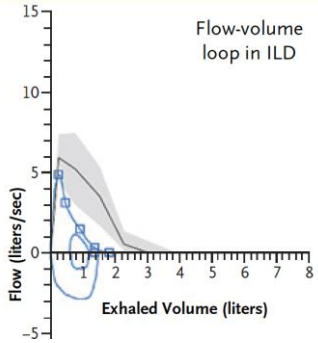

*D'après Raghu G, AJRCCM 2022, 205:e18; Visjenbeeck M, N Engl J Med 2020, 383:958*

# Evaluation pronostique des PID fibrosantes

♂



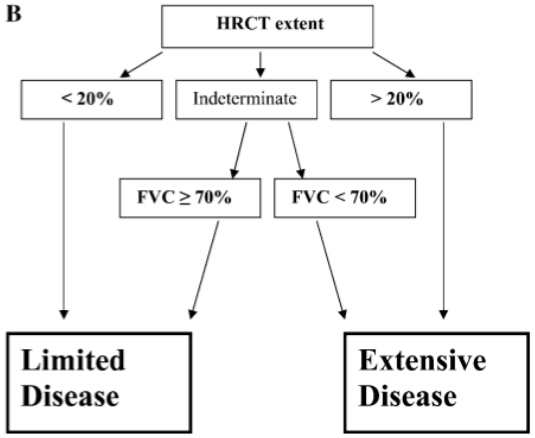
. UIP pattern
. Honeycombing




. FCV < 70%
. Honeycombing

## Others

. Etiology
. Black ethnicity
. Disease extension - SSc
. Recent vs old disease
. Particular antibodies
. Pulmonary hypertension
. Comorbidities
. Persistant exposure




### ILD-GAP score

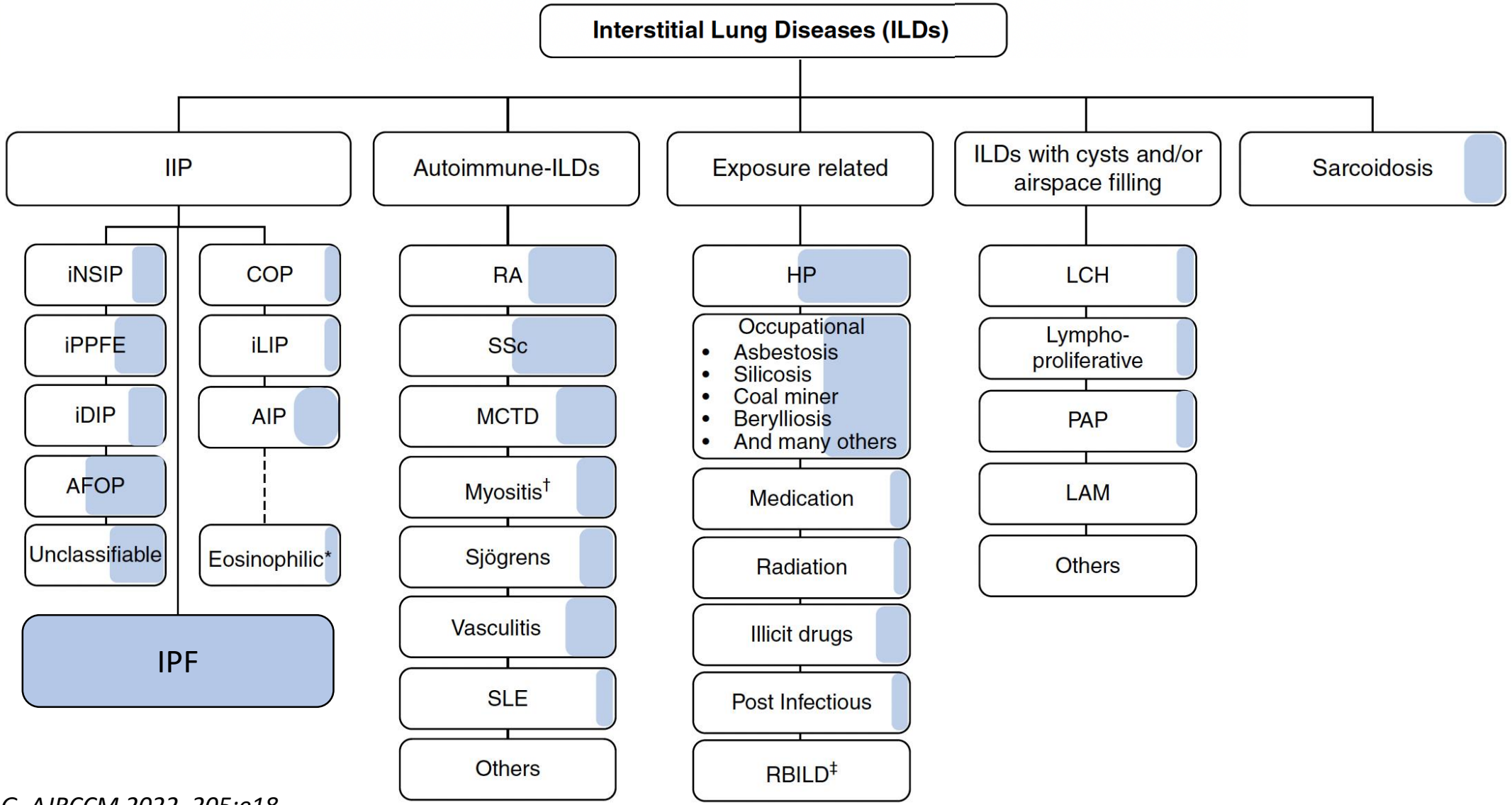
| | Facteurs prédictifs | Points |
|---|---|---|
| ILD | **Sous-type de PID** | |
| | FPI | 0 |
| | PID inclassable | 0 |
| | PID + connectivite/PINS idiopathique | –2 |
| | PHS | –2 |
| G | **Sexe** | |
| | Femme | 0 |
| | Homme | 1 |
| A | **Âge** | |
| | ≤ 60 ans | 0 |
| | 61-65 ans | 1 |
| | > 65 ans | 2 |
| P | **Physiologie** | |
| | CVF, % théorique | |
| | > 75 % | 0 |
| | 50-75 % | 1 |
| | < 50 % | 2 |
| | DLCO, % théorique | |
| | > 55 % | 0 |
| | 36-55 % | 1 |
| | ≤ 35 % | 2 |
| | Non réalisable | 3 |
| | **Total possible des points** | 8 |

**Mortalité prédite**

| Score ILD-GAP | 1 an | 2 ans | 3 ans |
|---|---|---|---|
| 0-1 | 3,1 | 6,6 | 10,2 |
| 2-3 | 8,8 | 18,0 | 26,9 |
| 4-5 | 18,2 | 35,0 | 49,2 |
| > 5 | 33,5 | 58,4 | 74,8 |

*D'après Raghu G, AJRCCM 2022, 205:e18; Visjenbeeck M, N Engl J Med 2020, 383:958*

# Mais où est l'ILA?

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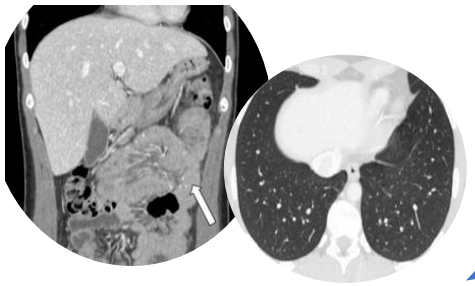
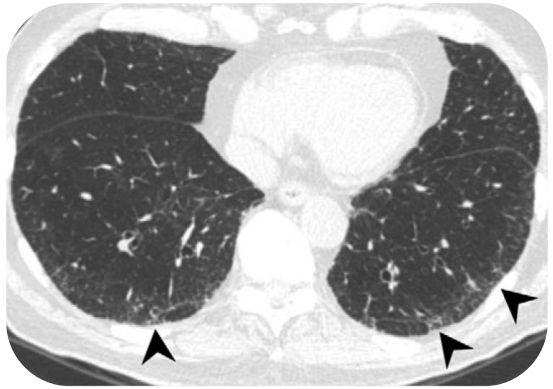
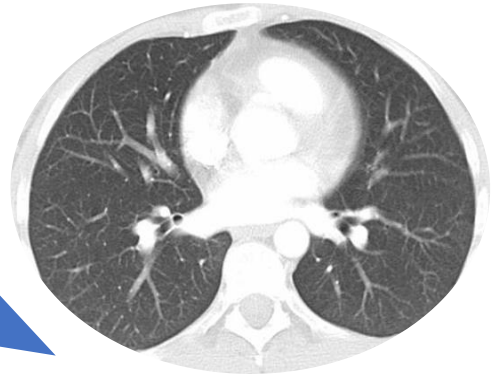


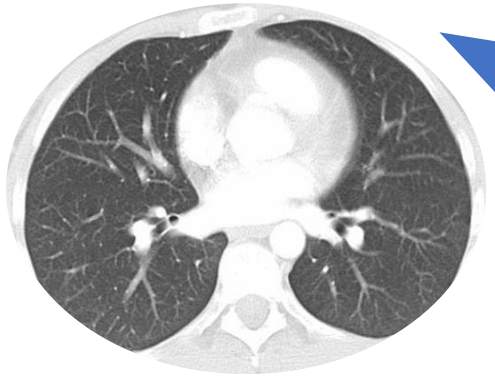
Extra-thoracic symptoms

**Incidental thoracic CT-scan**

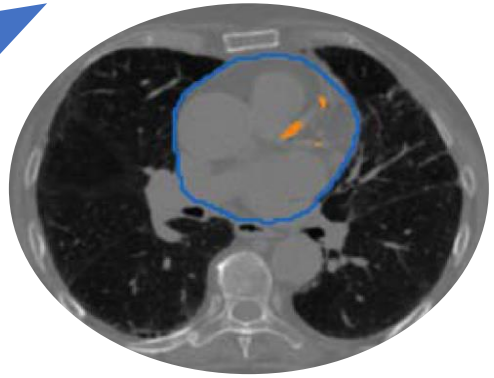




LC screening CT



Populational cohort



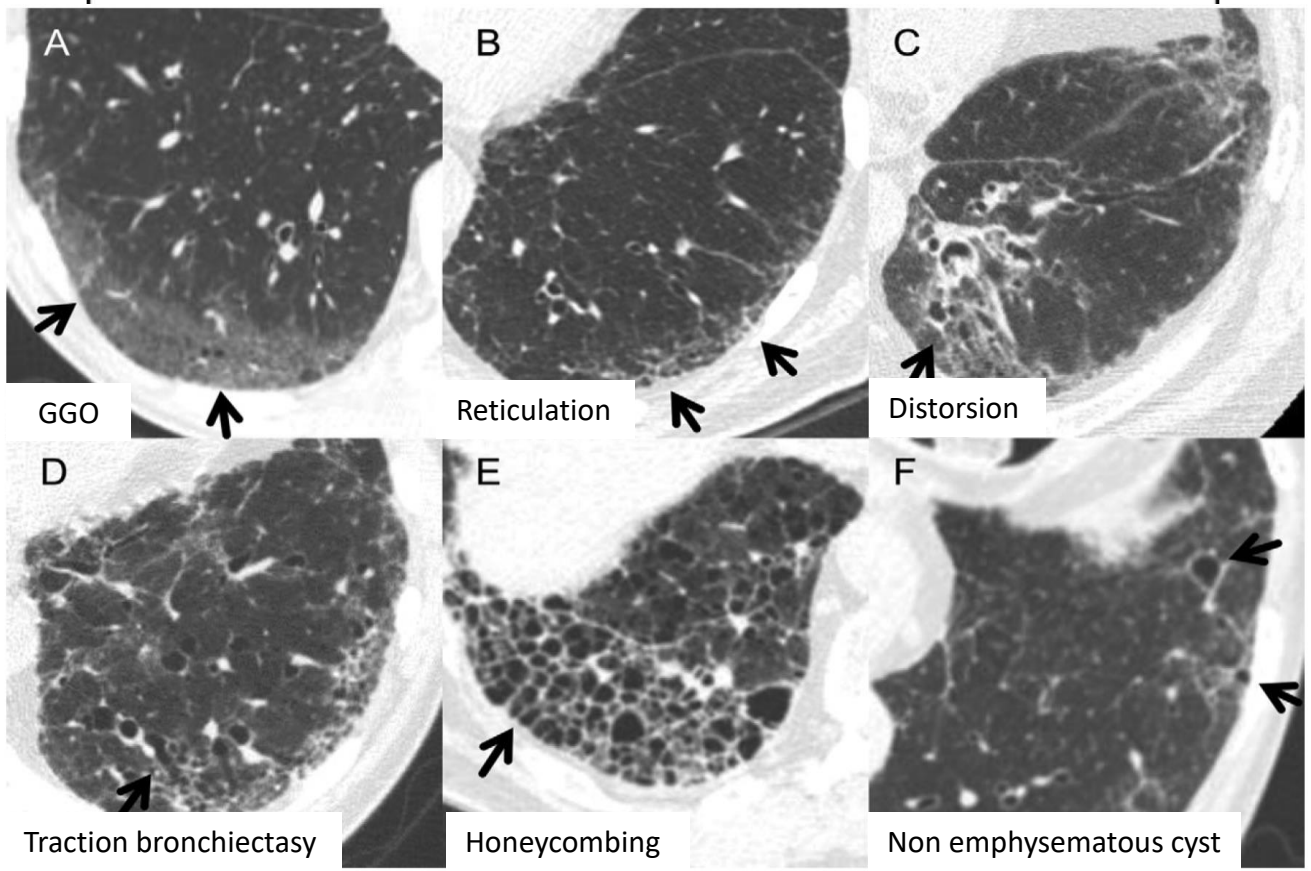
Coro-scan

# Définition de l'ILA… (1)

i) **Incidental**
ii) Procubitus CT
iii) Elementary lesions

**What is interstitial lung abnormality (ILA)?**

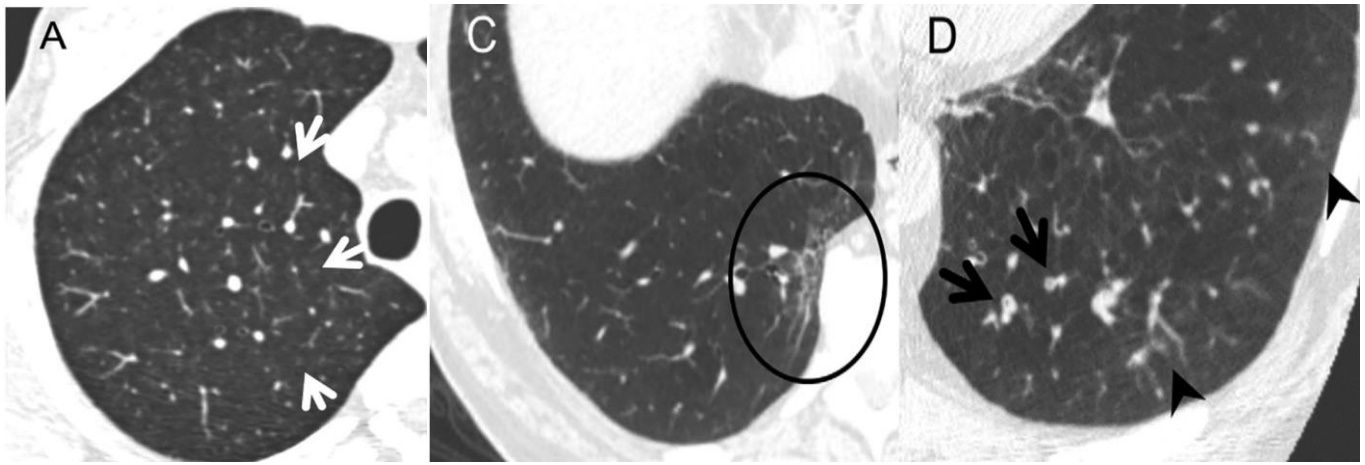
• Incidental identification of non-dependent abnormalities, including ground-glass or reticular abnormalities, lung distortion, traction bronchiectasis, honeycombing, and non-emphysematous cysts




*Hata A, Radiology 2021, 301:19*

# Définition de l'ILA… (2)

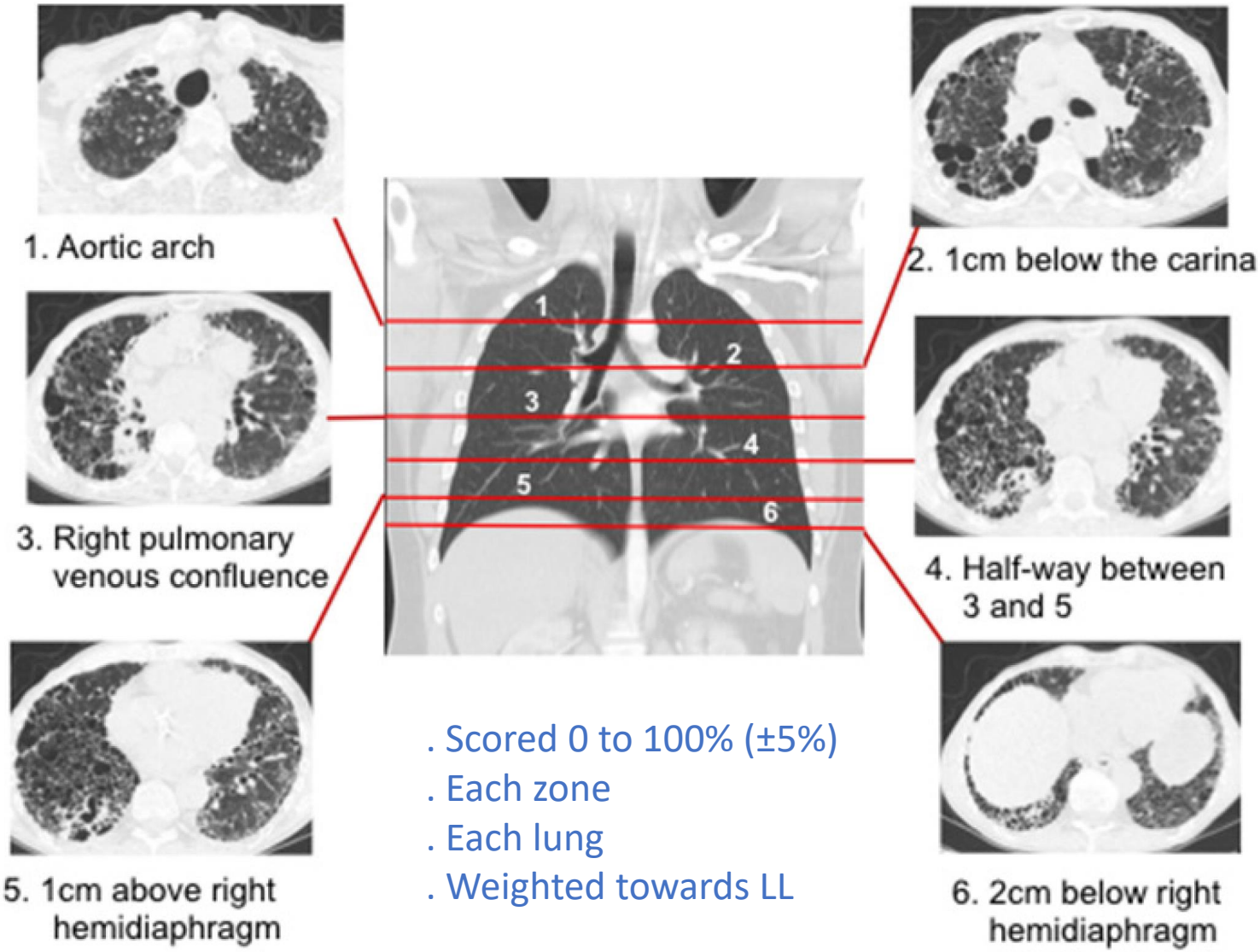
| CT Finding or Disease | |
|---|---|
| Basilar linear opacities | Non-ILA |
| Interlobular septal thickening because of interstitial edema | Non-ILA |
| Osteophyte-related fibrosis | Non-ILA |
| Aspiration | Non-ILA |
| Respiratory bronchiolitis | Non-ILA |




*Hata A, Radiology 2021, 301:19; Fraser E, BMJ Open Respir Res 2020, 7/000584*

# Définition de l'ILA… (3)

i) **Incidental**
ii) Procubitus CT
iii) Elementary lesion
iv) Eliminate non ILA
v) >5% of a lung zone but less than?




. Scored 0 to 100% (±5%)
. Each zone
. Each lung
. Weighted towards LL

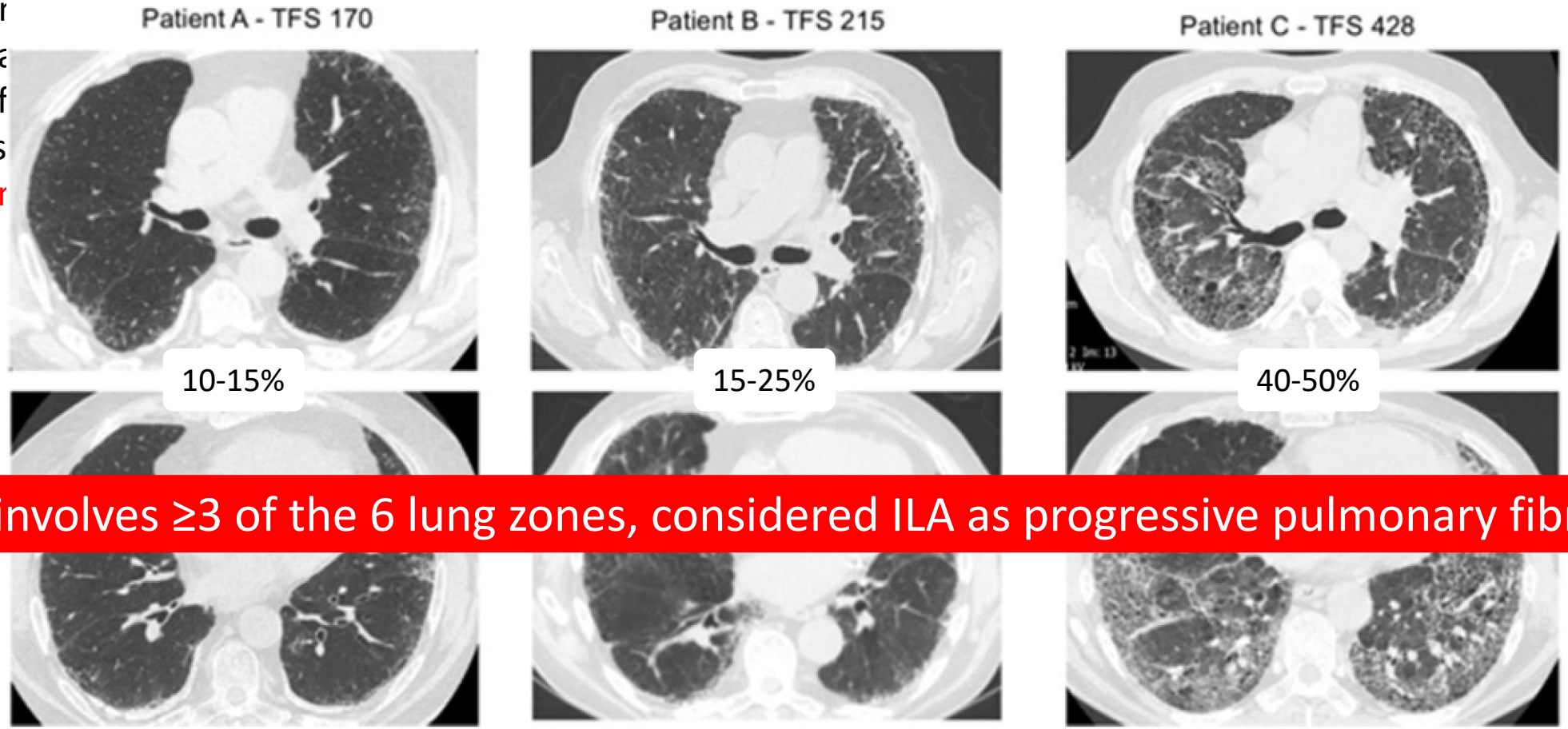
*Hata A, Radiology 2021, 301:19; Fraser E, BMJ Open Respir Res 2020, 7/000584*

# Définition de l'ILA… (4)

i) **Incidental**
ii) Procubitus CT
iii) Elemer
iv) Elimina
v) >5% of
but les
vii) Don't r

**What is interstitial lung abnormality (ILA)?**

• Incidental identification of non-dependent abnormalities,

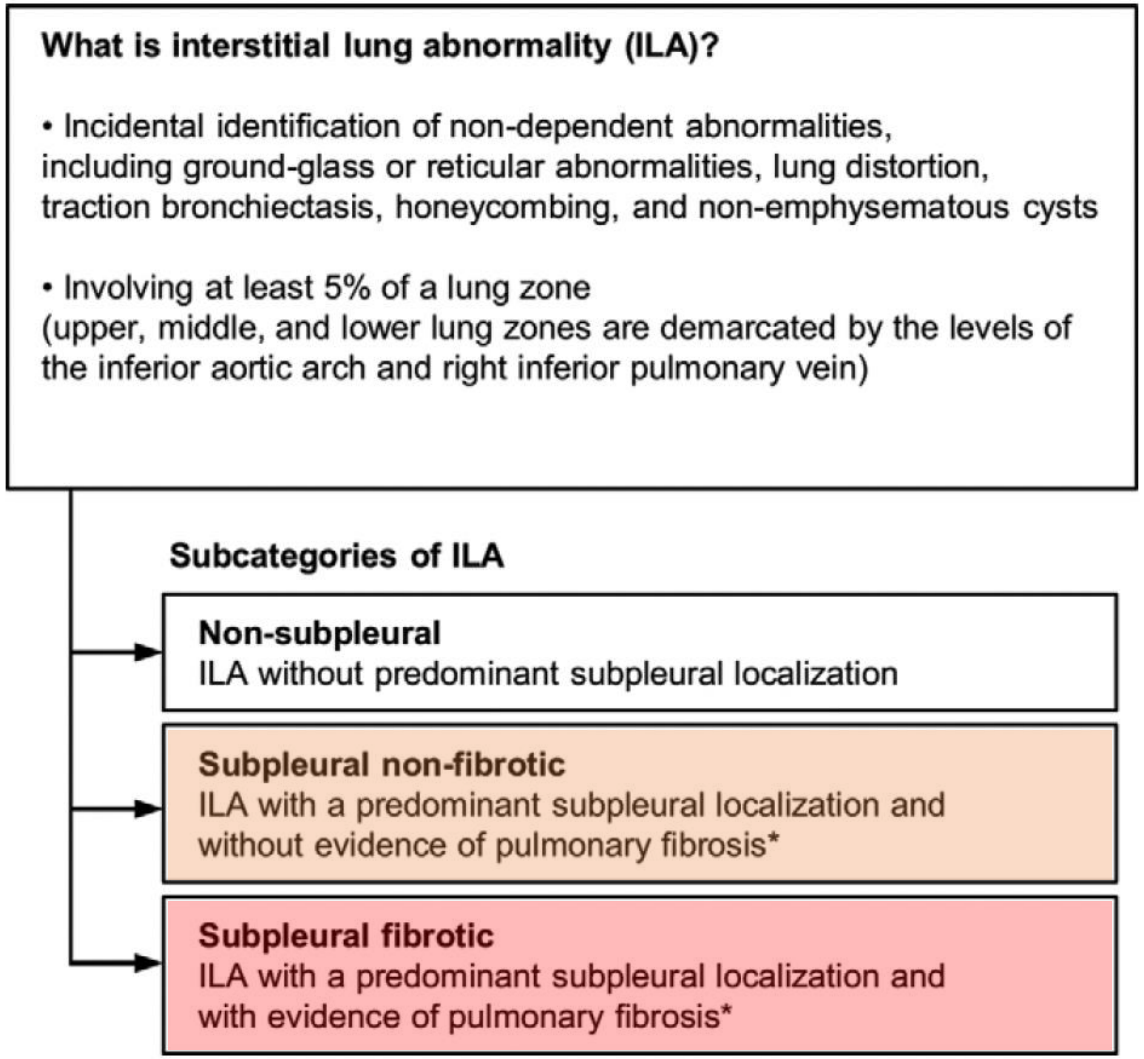



If ILA involves ≥3 of the 6 lung zones, considered ILA as progressive pulmonary fibrosis

*Hata A, Radiology 2021, 301:19; Fraser E, BMJ Open Respir Res 2020, 7/000584*

# Définition de l'ILA… (5)

i) **Incidental**
ii) Procubitus CT
iii) Elementary lesions
iv) Eliminate non ILA lesions
v) >5% of a lung zone, but less than?
vii) Don't miss PPF
viii) Subcategorize ILA



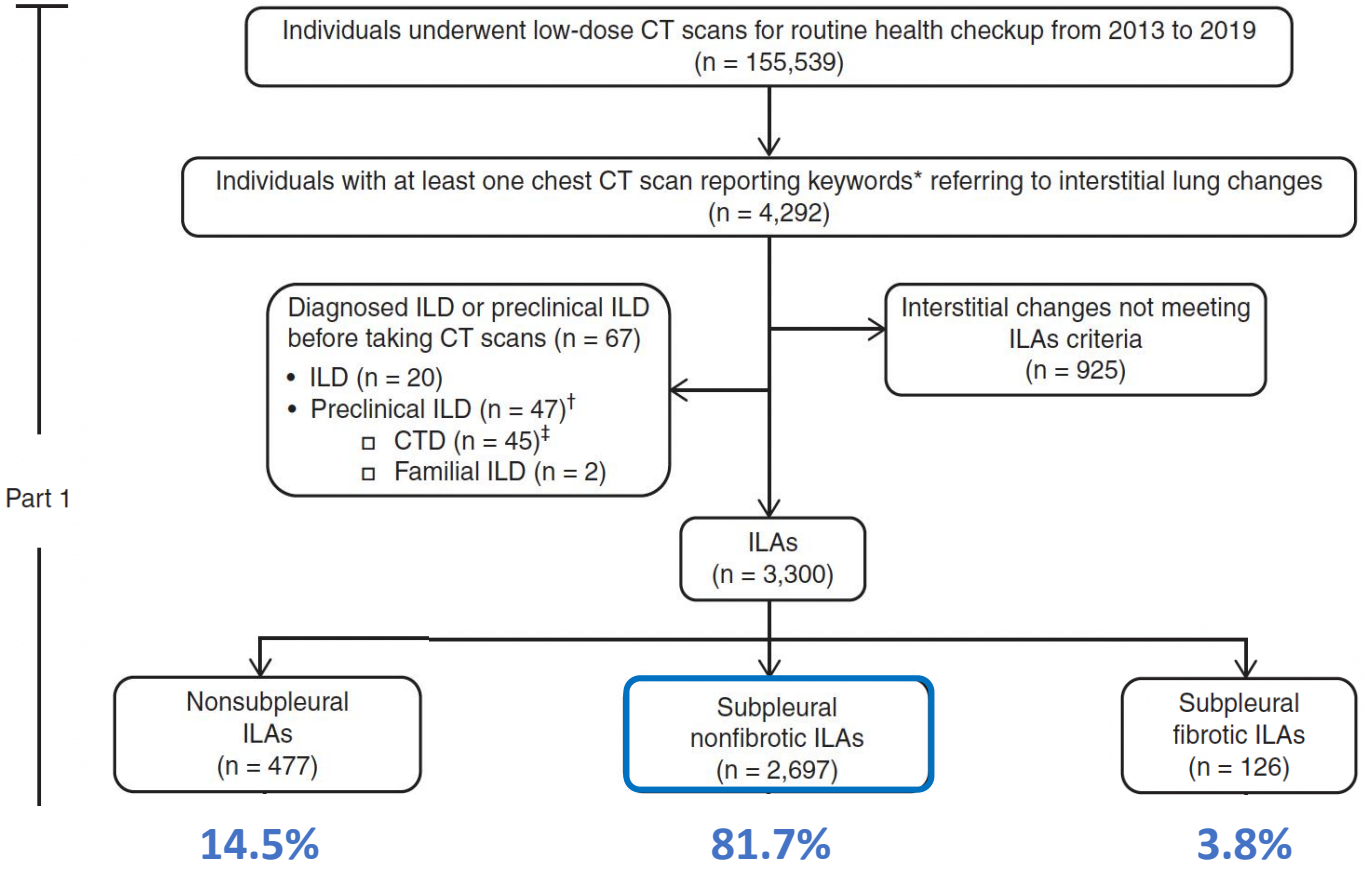

*Hata A, Radiology 2021, 301:19; Fraser E, BMJ Open Respir Res 2020, 7/000584;*

# Définition de l'ILA… (6)

i) **Incidental**
ii) Procubitus CT
iii) Elementary lesions
iv) Eliminate non ILA lesions
v) >5% of a lung zone, but less than?
vii) Don't miss PPF
viii) Subcategorize ILA

**Reticulation Is a Risk Factor of Progressive Subpleural Nonfibrotic Interstitial Lung Abnormalities**

Yuchen Zhang[1,2,3*], Huajing Wan[1,2,3*], Luca Richeldi[4*], Min Zhu[1,2,3*], Yan Huang[5*], Xiaofeng Xiong[1,2,3], Junzhe Liao[1,2,3], Wenjun Zhu[1,2,3,6], Lingli Mao[1,2,3], Linrui Xu[1,2,3], Dongfan Ye[1,2,3], Ling Chen[1,2,3], Jia Liu[1,2,3], Linxi Fu[1,2,3], Liangyuan Li[1,2,3], Lan Lan[1,2,3], Ping Li[1,2,3], Lixia Wang[1,2,3], Xiaoju Tang[1,2,3], and Fengming Luo[1,2,3]




*Hata A, Radiology 2021, 301:19; Fraser E, BMJ Open Respir Res 2020, 7/000584; Zhang Y, Am J Respir Crit Care Med 2022, 206:178*

# L'ILA dans le spectre des PID

**TABLE 1** Simplified definitions

| Entity | | Population | Diagnostic criteria | Definition |
|---|---|---|---|---|
| **ILA** | | Only individuals without known or suspected ILD[#] | Clinical-radiological entity | Incidental finding of CT abnormalities affecting more than 5% of any lung zone |
| **Early ILD** | **Pre-clinical ILD** | Individuals at risk for ILD | Clinical-radiological-pathological entity | Any ILD in asymptomatic patients with preserved lung function |
| | **Subclinical ILD** | Individuals NOT at risk for ILD | | |
| **Mild ILD** | | All individuals | Clinical-radiological-pathological entity | Any clinically significant ILD with minor symptoms and/or trivial PFT abnormalities |

*Tomassetti S, Eur Respir Rev 2022, 31:210206*

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- **Connective tissue disorders**: i) all CTD in male/smokers; ii) Systemic scleroderma, diffuse form, recent onset, anti-Scl-70/PMScl ab; ii) Idiopathic inflammatory myopathy with anti-MDA5; iii) Sjögren with SSA ab.

- **Familial ILD**: 1st-degree relatives with familial pulmonary fibrosis have 15-20% risk of having ILD on systematic thoracic CT scan

*Tomassetti S, Eur Respir Rev 2022, 31:210206*

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- Clinical symptoms in ILA : i) cough (12-40%); ii) exercise dyspnea (15-60%); iii) crakles (<25%)
- PFTs : some with alterations

- If ILA involves ≥3 of the 6 lung zones, considered **as mild ILD**?

*Tomassetti S, Eur Respir Rev 2022, 31:210206*

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*Tomassetti S, Eur Respir Rev 2022, 31:210206*

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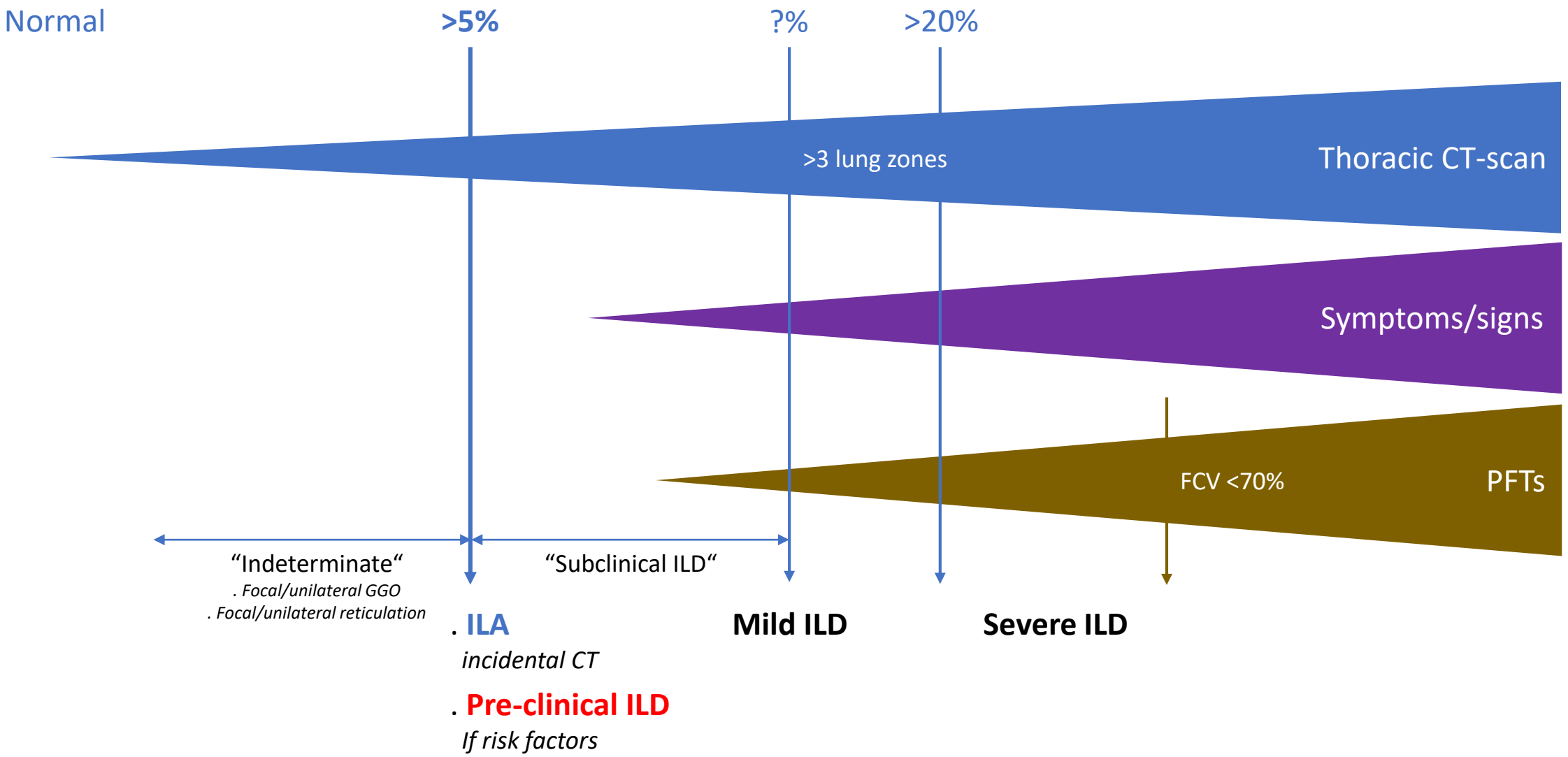

# Prévalence de l'ILA

**Table 1: Major Results of ILA Studies in Large Cohorts**

| Parameter | Population-based Cohorts | | | |
|---|---|---|---|---|
| | AGES-Reykjavik (9,18) | FHS (6,8,9) | MESA (11–14) | Nagano, Japan (15) |
| Sample size | 5320 | 2633 | 3137 | 3061 |
| Prevalence of ILA | 378 (7) | 177 (7) | 310 (10) | 80 (3) |
| Age (y)* | | | | |
| ILA group | 78 ± 6 | 70 ± 12 | NA | 62 ± 9 |
| Non-ILA group | 76 ± 5 | 56 ± 11 | NA | 54 ± 10 |
| Percentage of women (%) | | | | |
| ILA group | 172/378 (46) | 89/177 (50) | NA | 21/80 (26) |
| Non-ILA group | 1910/3216 (59) | 675/1370 (49) | NA | 1243/2981 (42) |
| Pack-years of smoking | | | | |
| ILA group | 11 (0–29)† | 19 (9–33)† | NA | 44 ± 26* |
| Non-ILA group | 0 (0–16)† | 11 (4–23)† | NA | 21 ± 13* |

*Hata A, Radiology 2021, 301:19*

**3 – 10%**

. **AGES**: Age, Gene/Environment Susceptibility; longitudinal **birth cohort** begin in 1967 including people born between 1907-1935

. **MESA(Lung)**: Multi-Ethnic Study of Atherosclerosis; cohort study included between 2000-2002 of 45 to 84 years persons from 6 USA communities without CV disases receiving **cardiac CT-scanning**

. **Nagano, Japan**: 2004 1yr Nagano Regional cohort of persons **concerned about their health**.

. **FHS**: Framingham Heart Study; designed to identfy **cardiovascular disease** in the general population

# Prévalence de l'ILA

**4 – 17%**

. **COPDGene**: Genetic Epidemiology of COPD longitudinal cohort; patients with active COPD, asthma and emphysema were excluded

. **ECLIPSE**: Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints

. **DLCST**: Danish Lung Cancer Screening Trial; persons at risk of lung cancer (age, smoking, COPD)

. **MILD**: Multicentric Italian Lung Detection; -Ethnic Study of Atherosclerosis; persons at risk of lung cancer (age, smoking, COPD)

. **NLST**: National Lung Screening trial; persons at risk of lung cancer (age, smoking, COPD)

**Table 1: Major Results of ILA Studies in Large Cohorts**

| | Smoking and Lung Cancer Screening Cohorts | | | | |
|---|---|---|---|---|---|
| Parameter | COPDGene (4,9,23) | DLCST (27) | ECLIPSE (9) | MILD (28) | NLST (7,16) |
| Sample size | 9292 | 1990 | 1670 | 692 | 884 |
| Prevalence of ILA | 708 (8) | 332 (17) | 157 (9) | 28 (4) | 86 (10) |
| Age (y)* | | | | | |
| ILA group | 64 ± 9 | 60 ± 5 | 64 ± 8 | 60 ± 6 | 62 ± 5 |
| Non-ILA group | 60 ± 9 | 58 ± 5 | 62 ± 7 | 57 ± 6 | 61 ± 5 |
| Percentage of women (%) | | | | | |
| ILA group | 345/708 (49) | 136/332 (41) | 41/157 (26) | 4/28 (14) | 27/86 (31) |
| Non-ILA group | 2457/5395 (46) | 742/1658 (45) | 182/528 (34) | 185/534 (35) | 295/696 (42) |
| Pack-years of smoking | | | | | |
| ILA group | 44 (30–64)† | 38 ± 13* | 43 (30–60)† | NA | 60 ± 29* |
| Non-ILA group | 40 (30–54)† | 36 ± 13* | 45 (33–62)† | NA | 51 ± 20* |

*Hata A, Radiology 2021, 301:19*

# Prévalence de l'ILA, âge et tabac dépendant

**Table 1: Major Results of ILA Studies in Large Cohorts**

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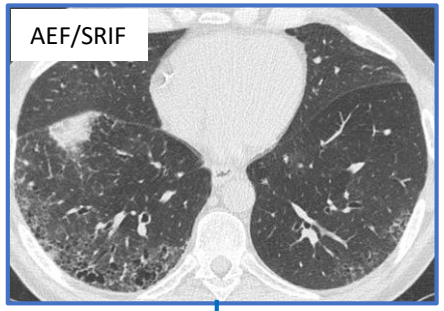
*Hata A, Radiology 2021, 301:19*

# Qu'il y a-t-il l'intérieur de l'ILA?

**Reviews…**




| Lung | | Radiologic Features |
|---|---|---|
| Smokers | Airspace enlargement with fibrosis, UIP, respiratory bronchiolitis, Langerhans cell histiocytosis, and nondescript interstitial changes | Nondependent ground-glass reticular abnormalities, centrilobular nodules, nonemphysematous cysts, traction bronchiectasis, honeycombing |
| Postoperative | Subpleural fibrotic lesions | Honeycombing, reticular shadow, ground-glass opacities |

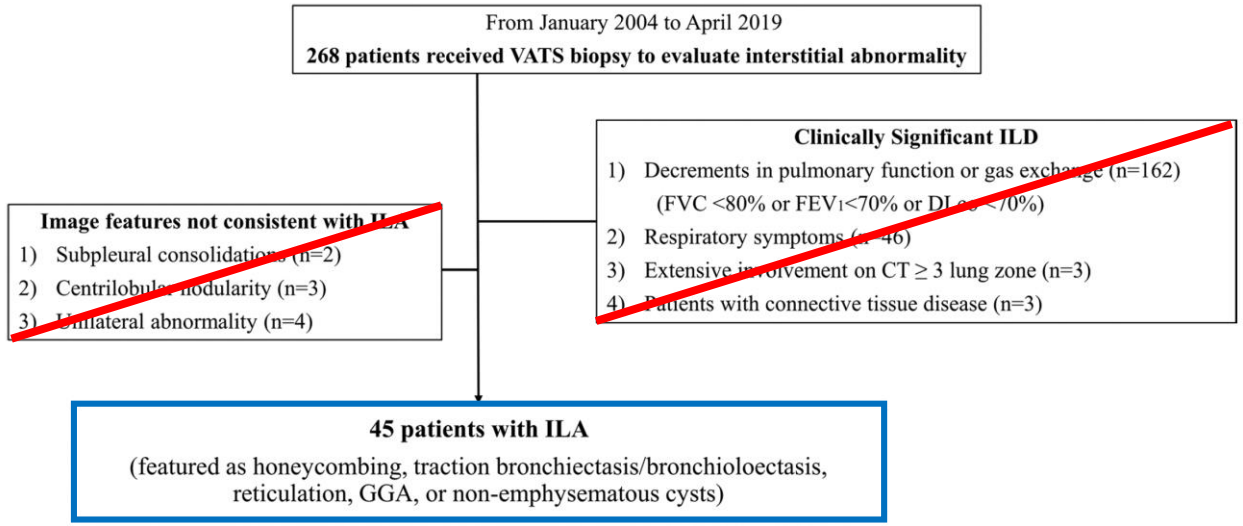
European Radiology (2022) 32:2713–2723
https://doi.org/10.1007/s00330-021-08378-8

CHEST

Check for updates

## Radiologic-pathologic correlation of interstitial lung abnormalities and predictors for progression and survival

Kum Ju Chae[1] · Myoung Ja Chung[2] · Gong Yong Jin[1] · Young Ju Song[1] · Ae Ri An[2] · Hyemi Choi[3] · Jin Mo Goo[4]



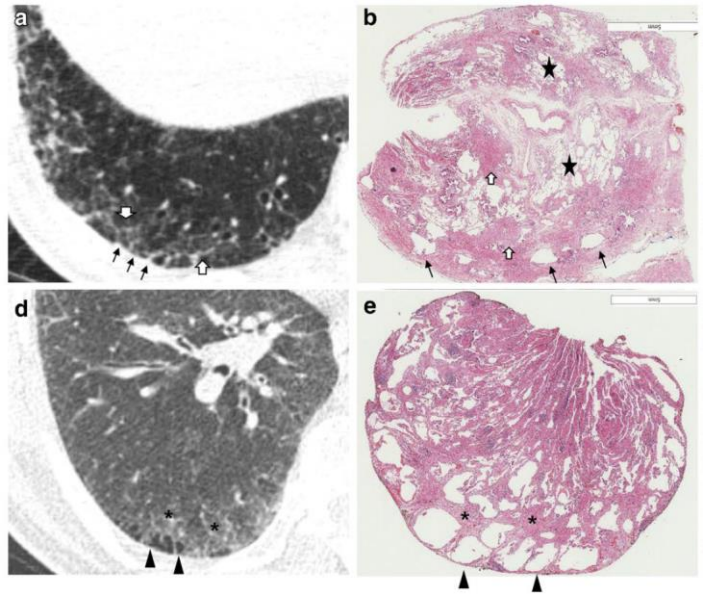

*Tracy J, Am J Respir Crit Care Med 2012, 185:1147; Hata A, Radiology 2021, 301:19; Hatabu H, Lancet Respir Med 2020, 8:728; Chae K, Eur Radiology 2022, 32:2713*

# Qu'il y a-t-il l'intérieur de l'ILA?

| Characteristics | Fibrotic-ILA ($n = 36$) | Non-Fibrotic ILA ($n = 9$) |
|---|---|---|
| No. of men | 30 (83) | 8 (89) |
| Age (years) | 71.9 ± 7.3 | 73.4 ± 7.6 |
| Smoking status | | |
| Never smoker | 16 (44) | 3 (33) |
| Current smoker | 9 (25) | 0(0) |
| Former smoker | 11 (31) | 6 (67) |
| Smoking intensity (pack-years) | 37.4 ± 9.4 | 41.7 ± 11.7 |
| PFT (% predicted) | | |
| FVC | 94.4 ± 13.6 | 95.5±8.7 |
| $FEV_1$ | 102.8 ± 23.5 | 103.1 ± 15.1 |
| $FEV_1$/FVC | 78.3 ± 5.7 | 95.5 ± 28.2 |
| FEF25-75% | 95.5 ± 28.2 | 83.3 ± 29.4 |

**Table 2** Radiologic-pathologic correlation according to the radiologic status of fibrotic ILA, non-fibrotic ILA

| Pathology | Radiology | | |
|---|---|---|---|
| | Fibrotic ILA ($n = 36$) | Non-fibrotic ILA ($n = 9$) | Overall ($n = 45$) |
| Definite UIP | 17 (47) | 1 (11) | 18 (40) |
| Probable UIP | 8 (22) | 0 (0) | 8 (18) |
| Indeterminate UIP | 8 (22) | 4 (44) | 12 (27) |
| Inconsistent with UIP | 3 (8) | 4 (44) | 7 (16) |




*Chae K, Eur Radiology 2022, 32:2713*

# Quels sont les facteurs de risques de l'ILA?

**Age**
. <60 yrs, 4% vs >70 yrs, 6%
. **x2.2**/10 yrs more old
. Plasma Growth factor 15: **x3.4** (TNF, CRP, IL-6)

**Environmental exposure**
. NO: **x1.65**/40 ppb
. PM 2.5: **x1.25**/0.14µg/m3/5 yrs
. Self reported exposure (vapours, gas, dusts): **x1.76**

**Sex?**
. 0 to x1.7 male vs female

**MUC5B**
. Minor allele (rs35705950): **x2.8**
. UIP pattern: **x2.7**

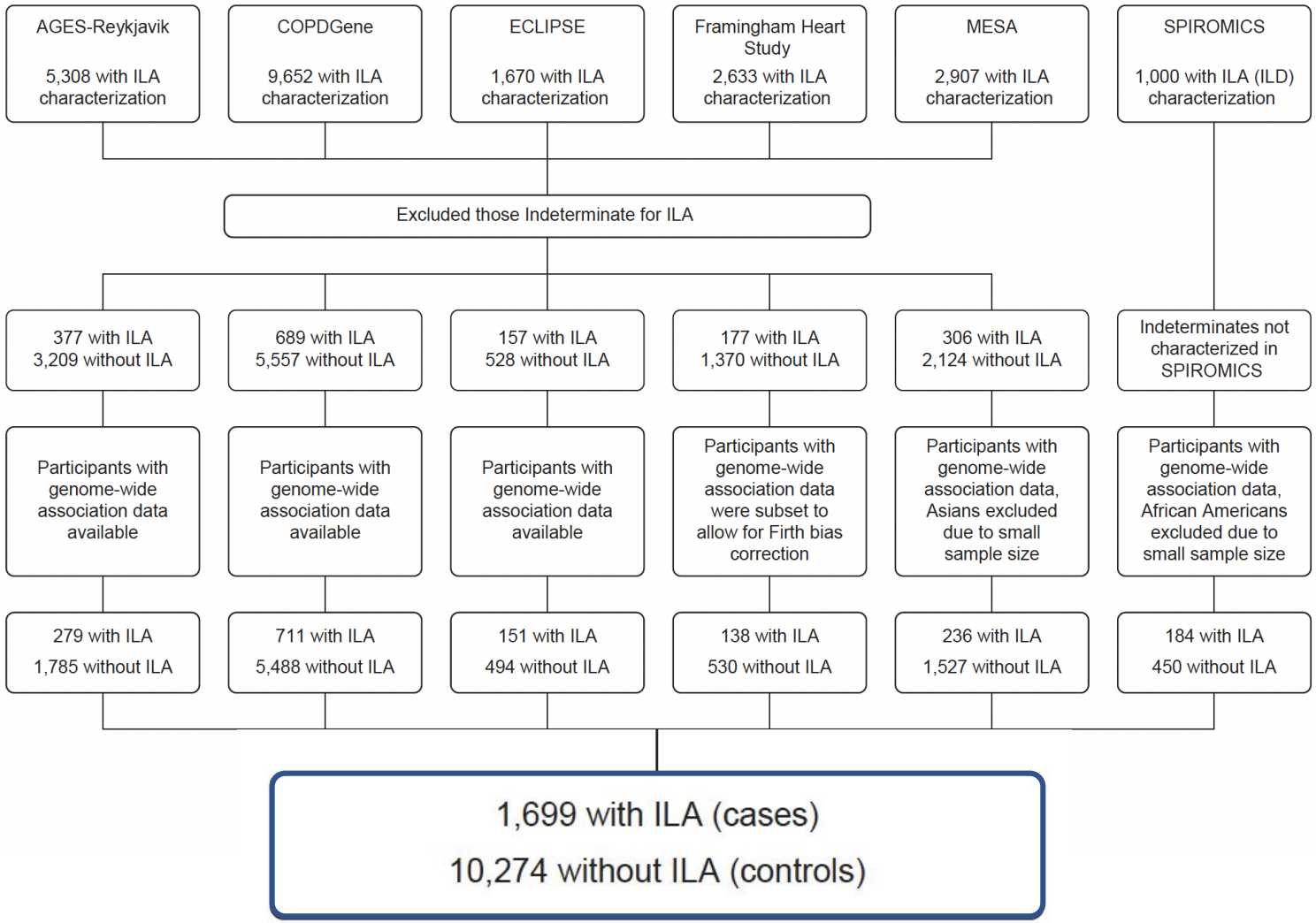
**Other mutations**
. DDP9, DSP, FAM12A, IVD (and IPF)
. IPO11, FC1P3 (but not IPF)
. HTRE1 (subpleural predominance)

**Smoking ±COPD**
. Smokers: **x2.2** ILA occurrence/10 yrs
. Current vs former: **x1.8**

**Immune and inflammation**
. CD4 cell proliferation, loss of KLRG1 expression
. Plasma MMPs and resistin

*Hatabu H, Lancet Respir Med 2020, 8:728; Hata A, Radiology 2021, 301:19; Tomasseti S, Eur Respir Rev 2022, 31:201206*

# Polymorphisme génétique et risque d'ILA?




*Hobs BD, Am J Respir Med Crit Care 2019, 200:1402*

# Polymorphisme génétique et risque d'ILA?

**Genes polymorphisms asso**

## Interstitial lung abnormalities are associated with decreased mean telomere length

Rachel K. Putman[1], Gisli Thor Axelsson[2,3], Samuel Y. Ash[1], Jason L. Sanders[1], Aravind A. Menon[1], Tetsuro Araki[4,5], Mizuki Nishino[4,5], Masahiro Yanagawa[6], Elías F. Gudmundsson[3], Dandi Qiao[7], Raúl San José Estépar[4], Josée Dupuis[8], George T. O'Connor[9], Ivan O. Rosas[10], George R. Washko[1], Souheil El-Chemaly[1], Benjamin A. Raby[1,11], Vilmundur Gudnason[3], Dawn L. DeMeo[7], Edwin K. Silverman[7], Hiroto Hatabu[4,5], Immaculata DeVivo[7,12], Michael H. Cho[1,7], Gunnar Gudmundsson[3,13] and Gary M. Hunninghake[1]

| Chromosome/ Location | rsID | IPF Risk Allele | | | | | | | Direction of Effect Consistent with Prior Reports |
|---|---|---|---|---|---|---|---|---|---|
| 4q22 | rs2609255 | G | | | | | | | Yes |
| 6p24 | rs2076295 | G | | | | | | | Yes |
| 11p15 | rs35705950 | T | | | | | | | Yes |
| 15q15 | rs2034650 | A | | | | | | | Yes |
| 19p13 | rs12610495 | G | | | | | | | Yes |
| 3q26 | rs6793295 | C | | | | | | | Yes |
| 17q21 | rs1981997 | G | | | | | | | Yes |
| 5p15 | rs2736100 | A | *TERT* | (7, 8) | 2.11 (1.61–2.78) | 1.03 (0.95–1.12) | 0.44 | 1.06 (0.96–1.16) | 0.23 | Yes |
| 10q24 | rs11191865 | A | *OBFC1* | (8) | 1.25 (1.15–1.35) | 1.03 (0.95–1.12) | 0.46 | 1.03 (0.94–1.13) | 0.56 | Yes |
| 13q34 | rs1278769 | G | *ATP11A* | (8) | 1.27 (1.14–1.39) | 1.04 (0.95–1.15) | 0.37 | 1.04 (0.94–1.16) | 0.45 | Yes |
| 15q25 | rs62025270 | A | *AKAP13* | (11) | 1.27 (1.18–1.37) | 1.09 (0.99–1.20) | 0.08 | 1.07 (0.96–1.20) | 0.23 | Yes |
| 7q22 | rs4727443 | C | *LOC100128334/ LOC105375423* | (8) | 1.30 (1.19–1.41) | 0.95 (0.87–1.03) | 0.19 | 0.93 (0.84–1.02) | 0.12 | No |

*Hobs BD, Am J Respir Med Crit Care 2019, 200:1402; Putman R, Eur Respir J 2022, 60:20101814*

# Polymorphisme génétique et risque d'ILA?

**Genes polymorphisms associated with increased risk of ILA, but not IPF?**

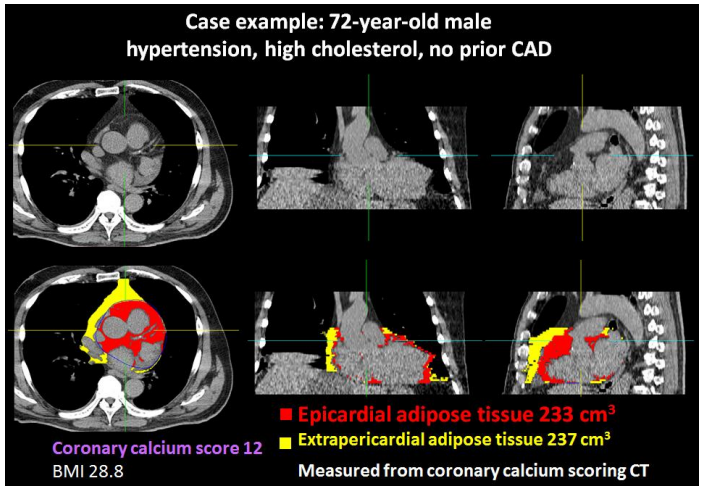
| Chromosome/ Location | Position | rsID | Risk Allele | Risk Allele Frequency | Nearest Gene | ILA vs. No ILA | | Subpleural ILA vs. No ILA | | Replication in IPF Cohort | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Odds Ratio* (95% CI) | *P* Value | Odds Ratio (95% CI) | *P* Value | Odds Ratio (95% CI) | *P* Value |
| 3q13 | 106571023 | rs73199442 | T | 0.06 | *FCF1P3* | 1.68 (1.39–2.02) | $5 \times 10^{-8}$ | 1.61 (1.31–1.99) | $7 \times 10^{-6}$ | 0.98 (0.85–1.12) | 0.73 |
| 5q12 | 62172476 | rs6886640 | G | 0.62 | *IPO11* | 1.28 (1.18–1.41) | $4 \times 10^{-8}$ | 1.27 (1.14–1.40) | $8 \times 10^{-6}$ | 1.06 (0.99–1.14) | 0.11 |
| 6q15 | 87737841 | rs7744971 | G | 0.28 | *HTR1E* | 1.26 (1.16–1.37) | $1 \times 10^{-7}$ | 1.32 (1.19–1.45) | $4 \times 10^{-8}$ | 1.01 (0.94–1.09) | 0.75 |
| 11p15 | 1241221 | rs35705950 | T | 0.11 | *MUC5B* | 1.97 (1.74–2.22) | $3 \times 10^{-27}$ | 2.22 (1.93–2.55) | $2 \times 10^{-29}$ | 4.84 (4.37–5.36) | $1 \times 10^{-203}$ |

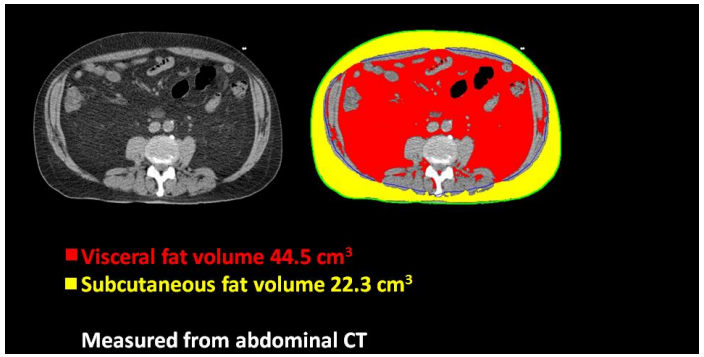
*Hobs BD, Am J Respir Med Crit Care 2019, 200:1402*

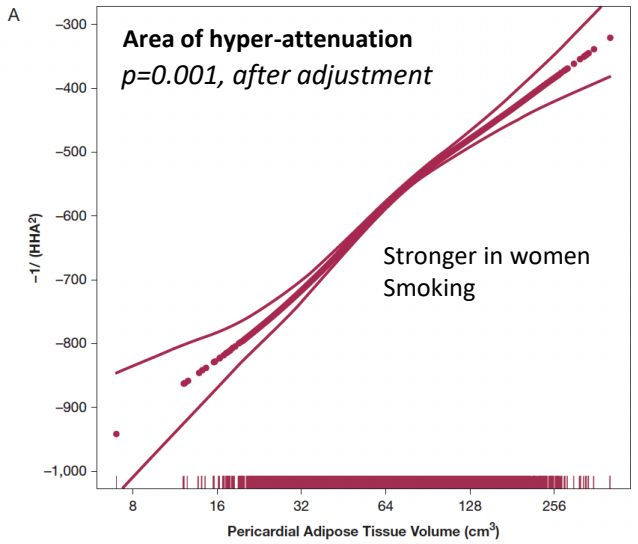
# Adiposité, adipokine et risque d'ILA?

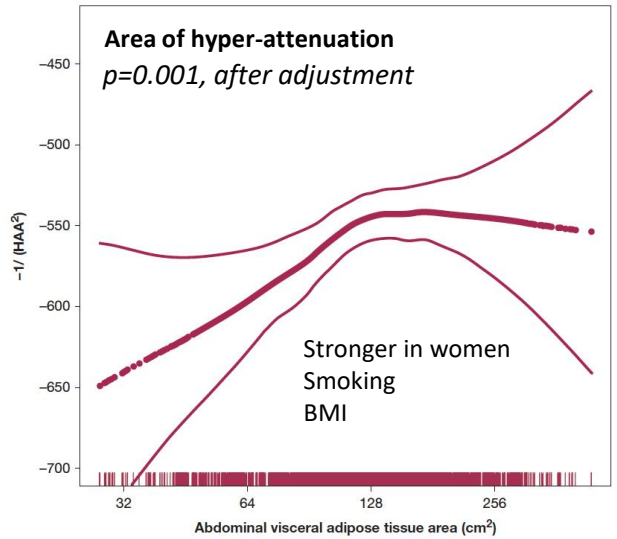
## MESA cohort

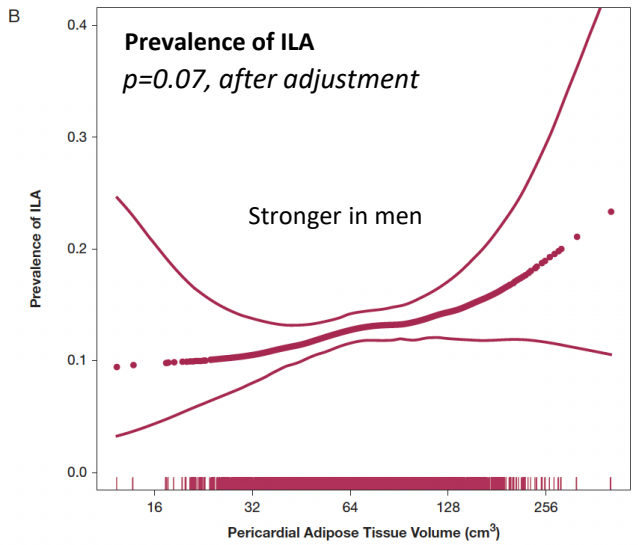
*. 6814 subjects received cardiac CT-scan*
*. 6784 with HAA/ILA evaluation*
*. 1923 received abdominal CT-scan*

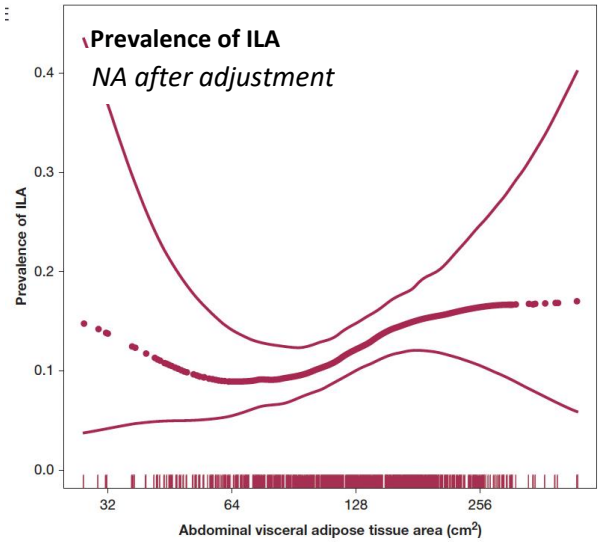


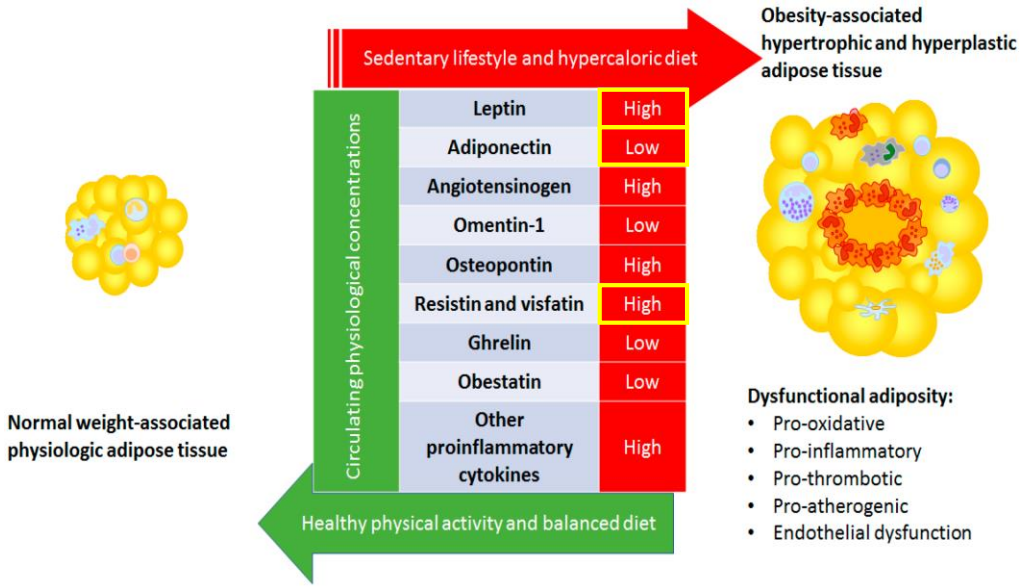

*Anderson M, Chest 2021, 160:582; Kim J, Chest 2020, 157:380*

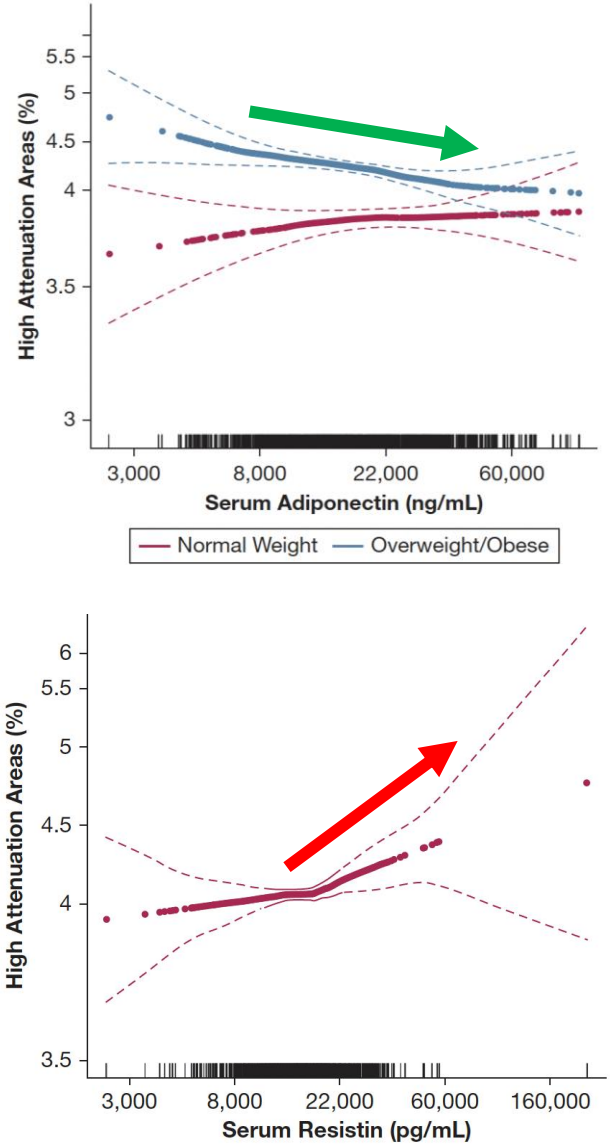
# Adiposité, adipokine et risque d'ILA?

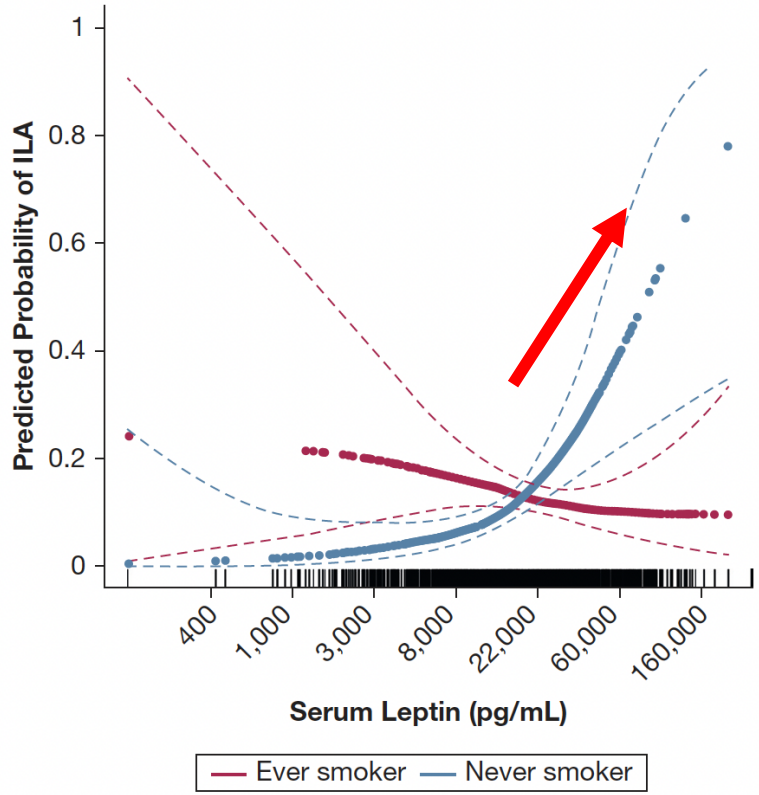
**MESA cohort**

*. 6814 subjects received cardiac CT-scan*

*. 1968 subjects with adiponectin, leptin, resistins serum evaluation*




*Anderson M, Chest 2021, 160:582; Kim J, Chest 2020, 157:380*

# Quelle est l'histoire naturelle de l'ILA?

**Table 1: Major Results of ILA Studies in Large Cohorts**

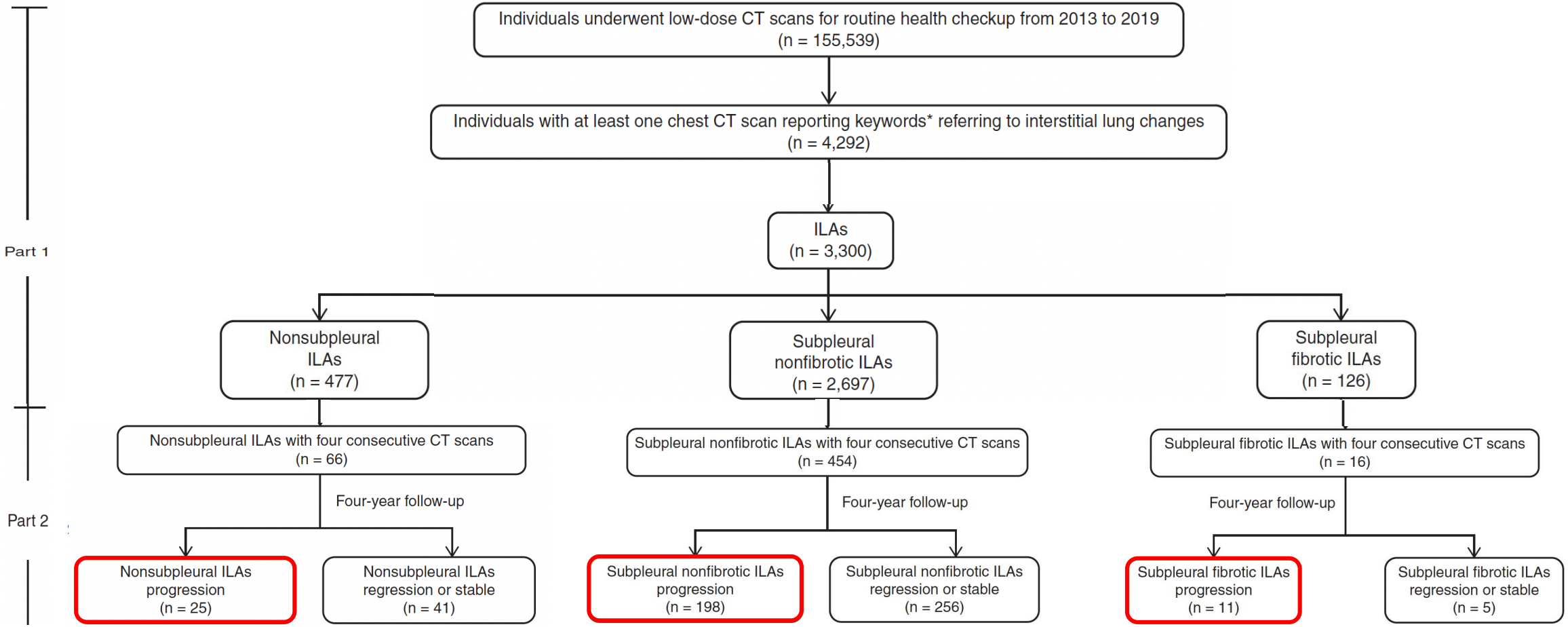
| | Population-based Cohorts | | | | Smoking and Lung Cancer Screening Cohorts | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Parameter | AGES-Reykjavik (9,18) | FHS (6,8,9) | MESA (11–14) | Nagano, Japan (15) | COPDGene (4,9,23) | DLCST (27) | ECLIPSE (9) | MILD (28) | NLST (7,16) |
| Sample size | 5320 | 2633 | 3137 | 3061 | 9292 | 1990 | 1670 | 692 | 884 |
| Prevalence of ILA | 378 (7) | 177 (7) | 310 (10) | 80 (3) | 708 (8) | 332 (17) | 157 (9) | 28 (4) | 86 (10) |
| Overall ILA progression (%) | 73 | 43 | NA | 44 | NA | NA | NA | NA | 20 |
| Follow-up time (y) | 5 | 6 | NA | 4 | NA | NA | NA | NA | 2 |
| Hazard ratio of mortality‡ | 1.3 (1.2, 1.4) | 2.7 (1.1, 6.5) | NA | NA | 1.8 (1.1, 2.8) | 2.0 (1.4, 2.7) | 1.4 (1.1, 2.0) | NA | NA |

*Hata A, Radiology 2021, 301:19*

# Quelle est l'histoire naturelle de l'ILA?

**Reticulation Is a Risk Factor of Progressive Subpleural Nonfibrotic Interstitial Lung Abnormalities**

Yuchen Zhang[1,2,3*], Huajing Wan[1,2,3*], Luca Richeldi[4*], Min Zhu[1,2,3*], Yan Huang[5*], Xiaofeng Xiong[1,2,3], Junzhe Liao[1,2,3], Wenjun Zhu[1,2,3,6], Lingli Mao[1,2,3], Linrui Xu[1,2,3], Dongfan Ye[1,2,3], Ling Chen[1,2,3], Jia Liu[1,2,3], Linxi Fu[1,2,3], Liangyuan Li[1,2,3], Lan Lan[1,2,3], Ping Li[1,2,3], Lixia Wang[1,2,3], Xiaoju Tang[1,2,3], and Fengming Luo[1,2,3]




**38%** **44%** **69%**

*Zhang Y, Am J Respir Crit Care Med 2022, 206:178*

# Quelle est l'histoire naturelle de l'ILA?

**AGES-Reykjavik study**

A: Associations between Imaging Features and ILA Progression

| Imaging Feature | Adjusted OR* | *P* Value |
|---|---|---|
| Centrilobular nodules | 0.2 (0.1, 0.5) | .0002† |
| Subpleural reticular markings | 6.6 (2.3, 19) | .0004† |
| Nonemphysematous cysts | 2.5 (1.3, 5.1) | .009† |
| Lower lobe predominant changes | 6.7 (1.8, 25) | .004† |
| Traction bronchiectasis | 6.6 (2.3, 19) | .0004† |

B: Associations between Imaging Features and Mortality‡

| Imaging Feature | Adjusted HR§ | *P* Value |
|---|---|---|
| Reticular markings | 1.6 (1.0, 2.5) | .049† |
| Centrilobular nodules | 0.9 (0.7, 1.1) | .3 |
| Nonemphysematous cysts | 1.4 (1.1, 1.8) | .02† |
| Traction bronchiectasis | 1.6 (1.3, 2.1) | .0001† |
| Lower lobe predominant changes | 1.1 (0.6, 1.7) | .8 |
| Subpleural location | 1.6 (1.0, 2.7) | .05 |
| ILA without fibrosis | 1.2 (1.1, 1.3) | .0004† |
| ILA with fibrosis | 1.5 (1.3, 1.6) | <.0001† |
| Indeterminate for UIP | 1.2 (0.98, 1.5) | .07 |
| Probable UIP pattern | 1.9 (1.5, 2.5) | <.0001† |
| UIP pattern | 4.5 (2.8, 7.2) | <.0001† |

*Hata A, Radiology 2021, 301:19; Putman RK, Am J Respir Crit Care Med 2019, 200:175; Hida T, Eur J Radiol 2020, 129:109073*

# Quelle est l'histoire naturelle de l'ILA?

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*Hata A, Radiology 2021, 301:19; Putman RK, Am J Respir Crit Care Med 2019, 200:175; Hida T, Eur J Radiol 2020, 129:109073*

# Quelle est l'histoire naturelle de l'ILA?

**Framingham Heart Study**

**TABLE 2** Interstitial lung abnormality (ILA) risk factors for progression and mortality

| | ILA progression | Mortality | First author [ref.] |
|---|---|---|---|
| **Progressive ILA** | | HR 3.9 (95% CI 1.3–10.9) | Araki [15] |
| **MUC5B (rs35705950)** | OR 2.8 (95% CI 1.7–4.4) | | Araki [15] |

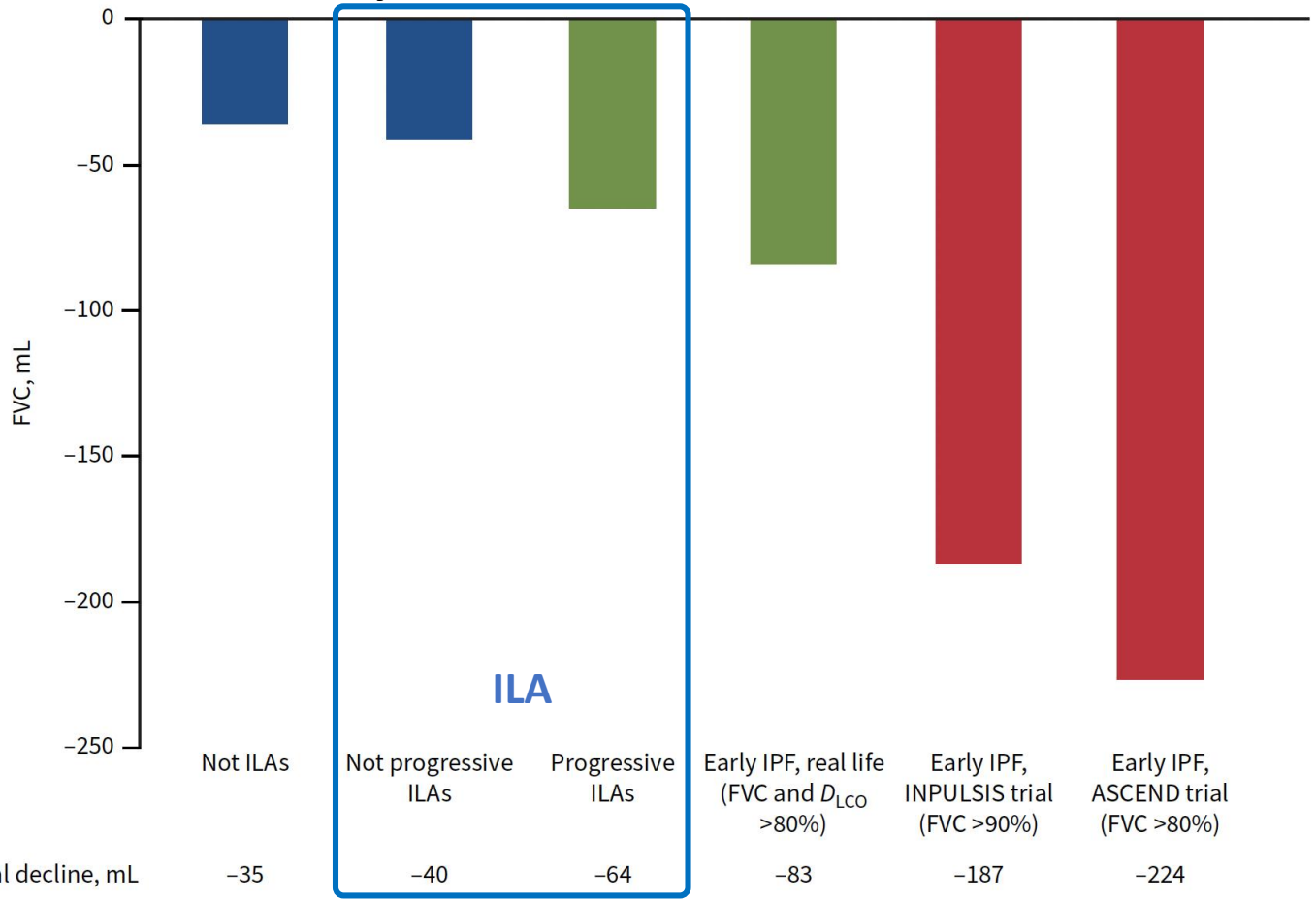
**Other risk factors of ILA progression**

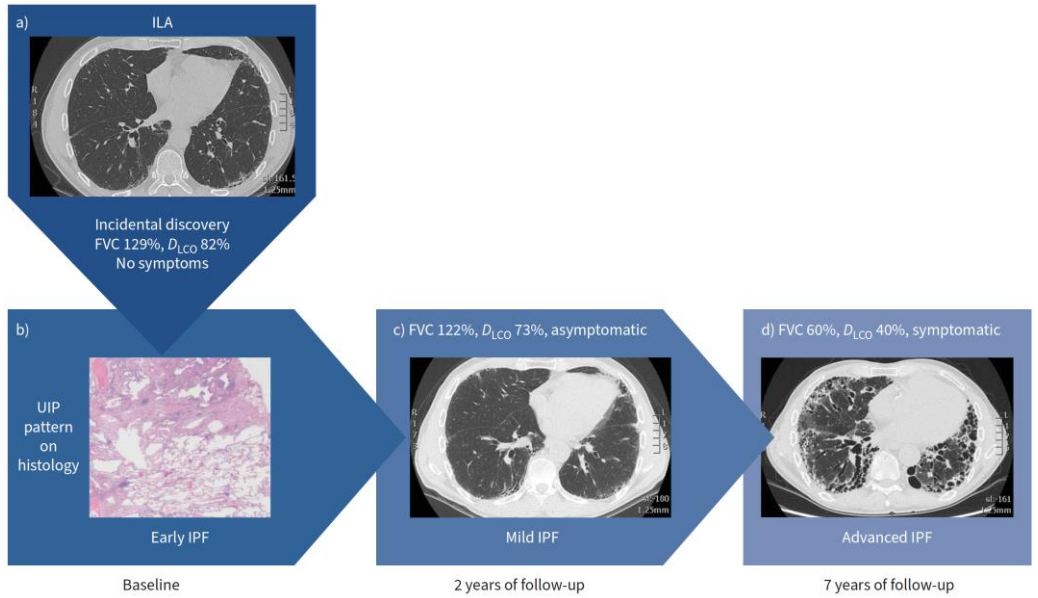
- Cigarette smoking
- Other inhalational exposures
- Medications (eg, chemotherapy, immune checkpoint inhibitors)
- Radiation therapy
- Thoracic surgery
- Physiological or gas exchange findings at lower limits of normal

*Tomassetti S, Eur Respir Rev 2022, 31:210206; Araki T, Am J Respir Crit Care Med 2016, 194:1514; Hatabu H, Lancet Respir Med 2020, 8:728*

# Quelle est l'histoire naturelle de l'ILA?

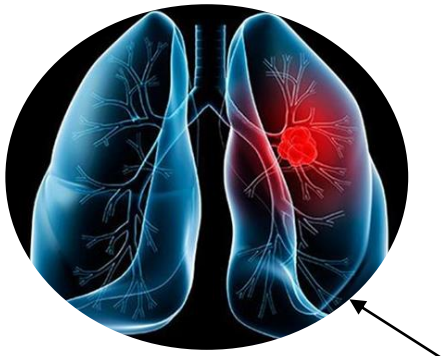
**Annual FVC decline in normal population, ILA, and control arm of early IPF in antifibrotic trials**



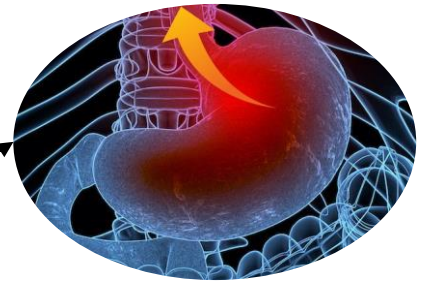




*Tomassetti S, Eur Respir Rev 2022, 31:210206; Araki T, Am J Respir Crit Care Med 2016, 194:1514*

# Quelles sont les comorbidités associées à l'ILA?

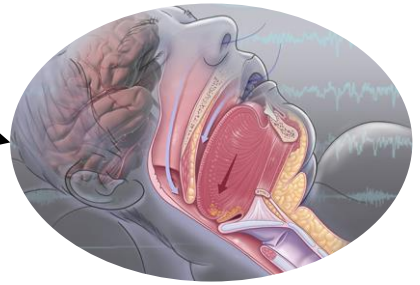


AGES, **HR: 2.17** (1.76-4.36)
NLST, **HR: 1.33** (1.07-1,65)



MESA, **OR: 1.78** (1.1-2.81);
young age, MUC5b allele

COPDgene, **OR: 1.17**; males



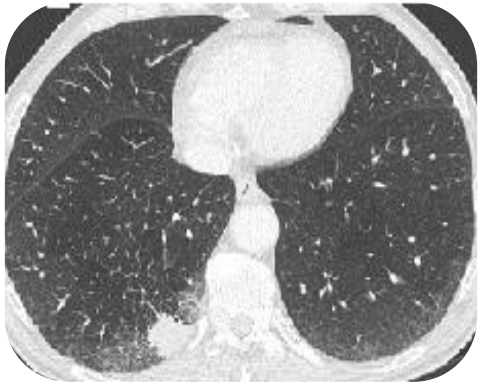
MESA, **OR: 1.35** (1.3-1.61);
BMI >30

*Tomassetti S, Eur Respir Rev 2022, 31:210206; Hata A, Radiology 2021, 301:19; Hatabu H, Lancet Respir Med 2020, 8:728; Kim S, Ann Am Thorac Soc 2017, 14:1786; Kim S, Eur Respir J 2022, in press*

# ILA et cancer du poumon, complications, mortalité

**Mortality**

. AGES, **HR: 2.89** (1.85-4.66)
. NLST, **HR: 1.51** (1.13-2.04)
. DLST, **HR: 3.2** (1.7-6.2)



**Post-operative complications**

. **OR: 1.91** (1.02-41.13)

**Radiation pneumonitis**

. 50-60 Gy Grade 3, **36%** vs 9%
. Stereotaxic radiation, **19%** vs 0%

**Mortality, per stage**

. Advanced stage, **HR: 2.09**
. Stage I, NSLT, **HR: 2.88**

**Immune related pneumonitis**

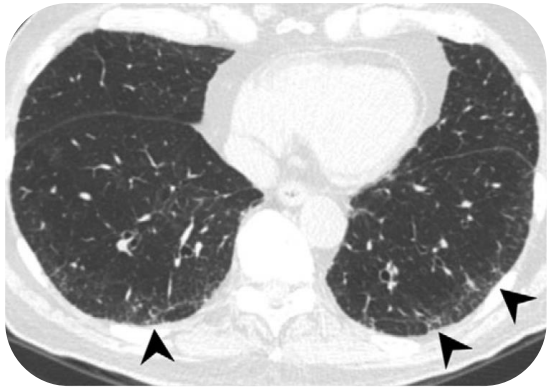
. **OR: 6.29** (2.3-16.92)

*Tomassetti S, Eur Respir Rev 2022, 31:210206; Hata A, Radiology 2021, 301:19; Hatabu H, Lancet Respir Med 2020, 8:728*

# ILA et comorbidités, complications, mortalité

**COPD**

. Exacerbations, **OR: 2.3**



**Systemic syndrome/sepsis**

. ARDS risk, **OR: 4.2** (2.1-8.2)

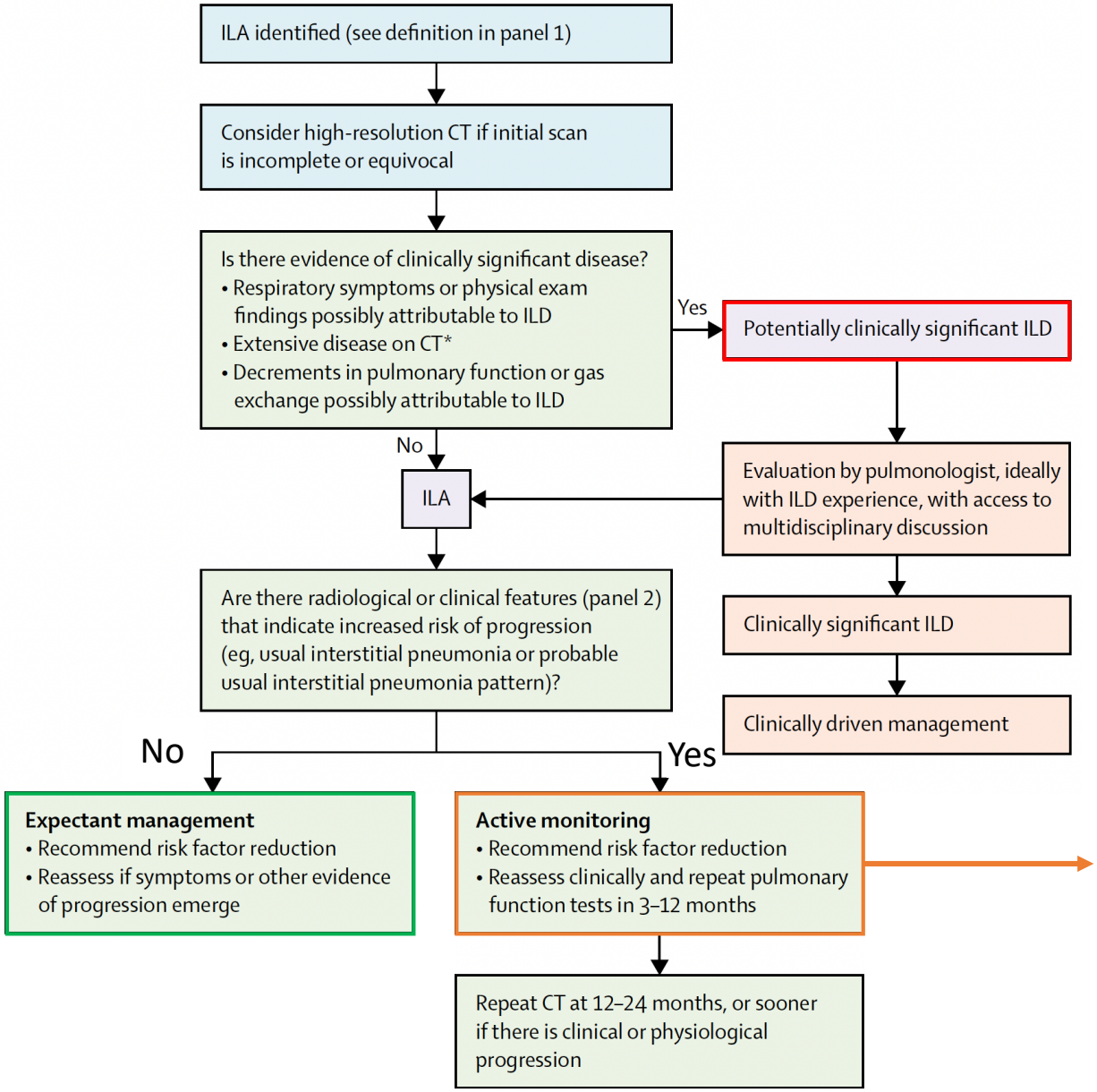
. ARDS mortality, **HR: 1.7** (1.2-2.3)

**Transcatheter aortic valve replacement**

. Mortality, **HR: 3.29** (1.34-8.08)

*Tomassetti S, Eur Respir Rev 2022, 31:210206; Hata A, Radiology 2021, 301:19; Hatabu H, Lancet Respir Med 2020, 8:728*

# Quelle prise en charge de l'ILA?




***Panel 2:* Risk factors for progression of interstitial lung abnormalities**

**Clinical risk factors**

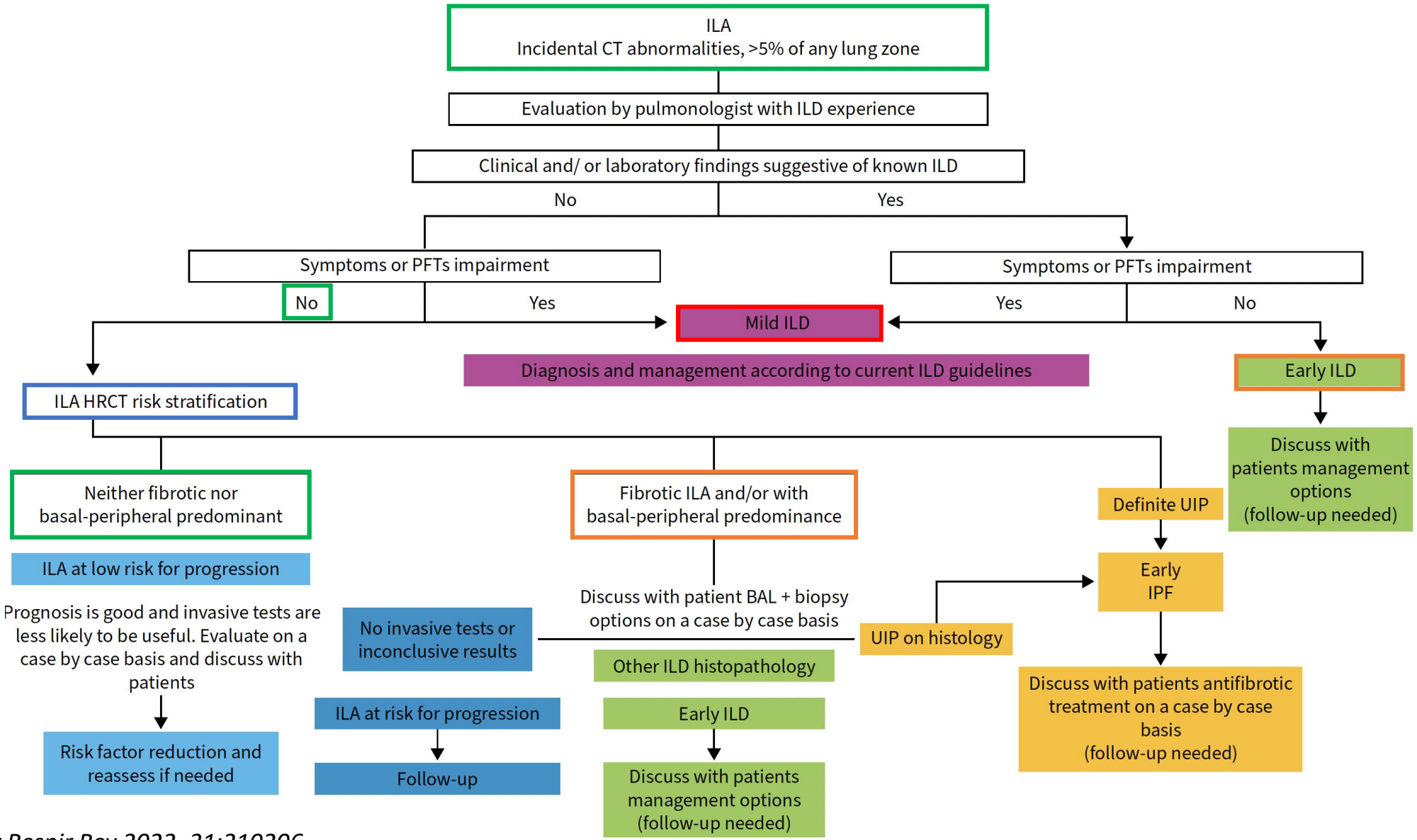
- Cigarette smoking
- Other inhalational exposures
- Medications (eg, chemotherapy, immune checkpoint inhibitors)
- Radiation therapy
- Thoracic surgery
- Physiological or gas exchange findings at lower limits of normal

**Radiological risk factors**

- Non-fibrotic interstitial lung abnormalities (ILAs) with basal and peripheral predominance
- Fibrotic ILAs with basal and peripheral predominance but without honeycombing (ILAs with probable usual interstitial pneumonia pattern)
- Fibrotic ILAs with basal and peripheral predominance and honeycombing (ILAs with usual interstitial pneumonia pattern)

*Hatabu H, Lancet Respir Med 2020, 8:728*

# Quelle prise en charge de l'ILA?



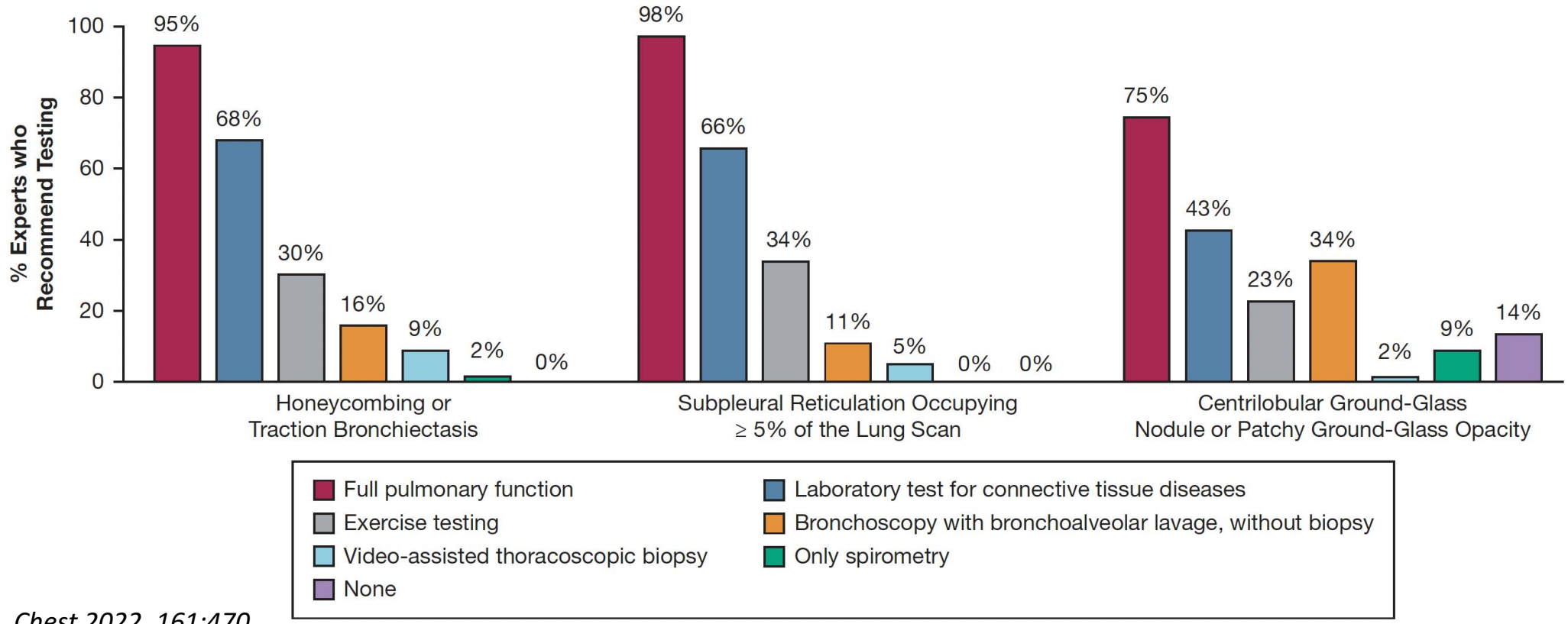

*Tomassetti S, Eur Respir Rev 2022, 31:210206*

# Quelle prise en charge de l'ILA?

## Detection and Early Referral of Patients With Interstitial Lung Abnormalities

### An Expert Survey Initiative

*Gary M. Hunninghake, MD, MPH; Jonathan G. Goldin, MD, PhD; Michael A. Kadoch, MD; Jonathan A. Kropski, MD; Ivan O. Rosas, MD; Athol U. Wells, MD, PhD; Ruchi Yadav, MD; Howard M. Lazarus, MD; Fereidoun G. Abtin, MD; Tamera J. Corte, MD, PhD; Joao A. de Andrade, MD; Kerri A. Johannson, MD, MPH; Martin R. Kolb, MD, PhD; David A. Lynch, MB, BCh; Justin M. Oldham, MD; Paolo Spagnolo, MD, PhD; Mary E. Strek, MD; Sara Tomassetti, MD; George R. Washko, MD; and Eric S. White, MD; on behalf of the ILA Study Group**




*Hunninghake G, Chest 2022, 161:470*

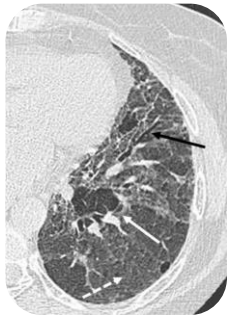
# ILA, quoi en faire en pratique ?

- Connaitre…
- La faire connaitre au non pneumologue
- Ne pas banaliser des anomalies interstitielles (fibrosante/sous-pleurale); en particulier en RCP d'oncologie thoracique
- Considérer le contexte familiale et de connectivite
- Aller au bout de la démarche diagnostique si symptômes et/ou étendue(?)
- Connaitre les facteurs de risque d'aggravation
- Et les prévenir, tabac, exposition, surpoids, GRD(?)
- Proposer une surveillance?

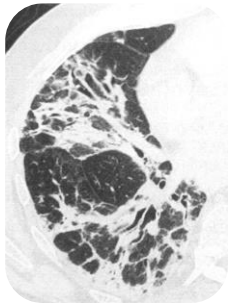
# Approche diagnostique des PID

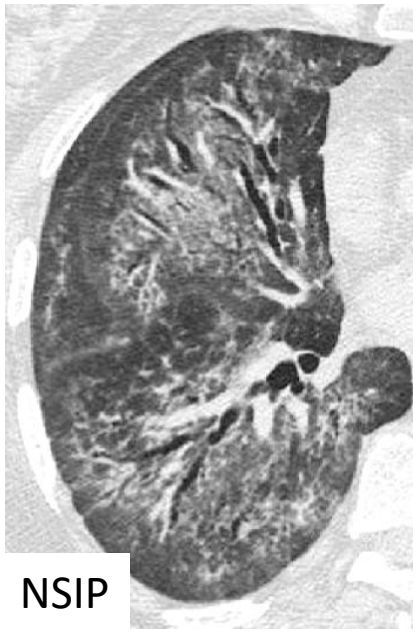
## Symptoms

HSP
RA
GS



IIM
Anti-Jo1

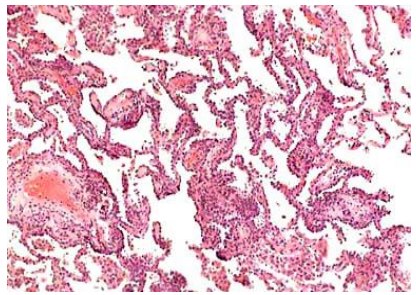




NSIP

UIP

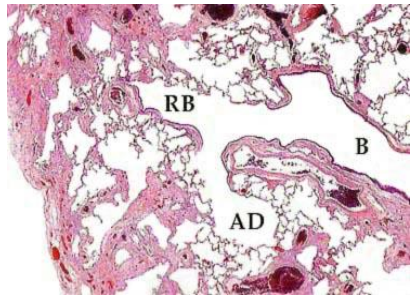
RA
MCTD
ANCA



Auto-immunity

- Systemic scleroderma
- RA, Sjögren
- MCTD

- Man
- >70 years old
- Smoker
- Clubbing
- “Velcro“ rales
- **IPF**



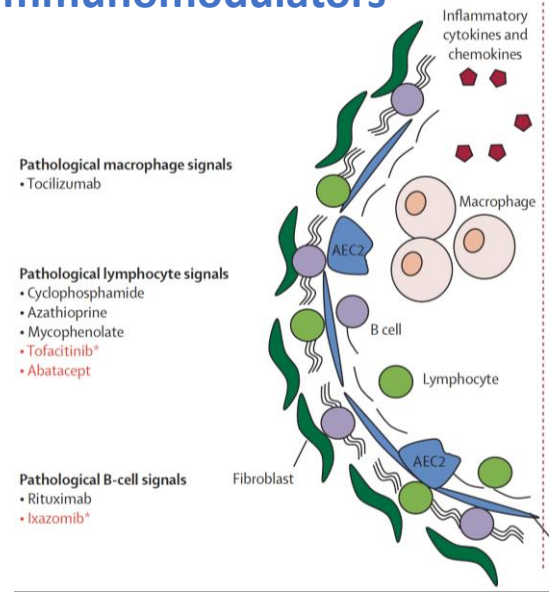

NSIP :
Non specific interstitial pneumonitis

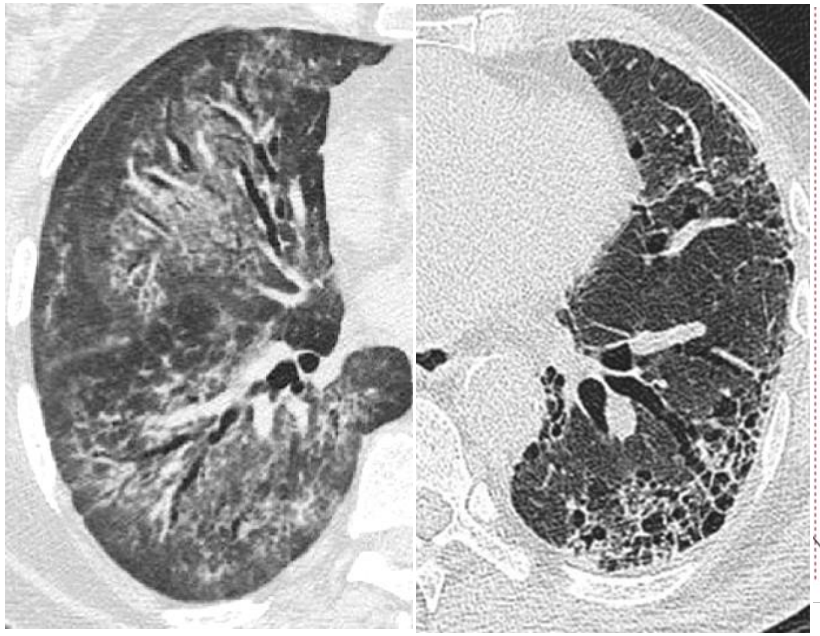
UIP :
Usual interstitial pneumonia

# Approche thérapeutique des PID

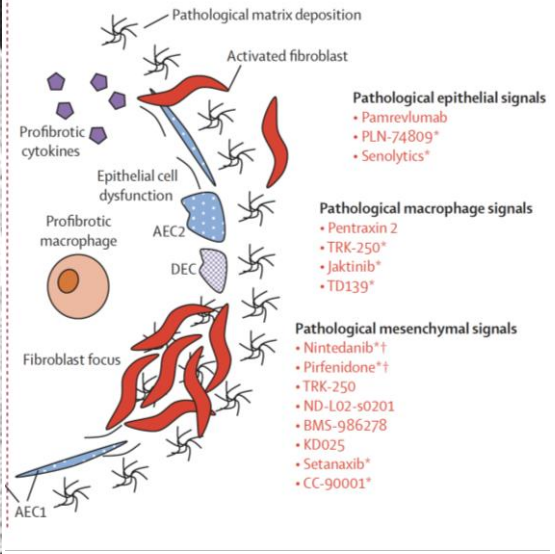
## Exposure exclusion

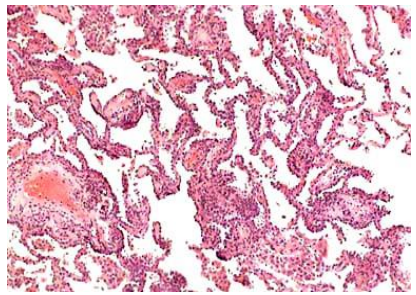
## Immunomodulators



## Fibromodulators



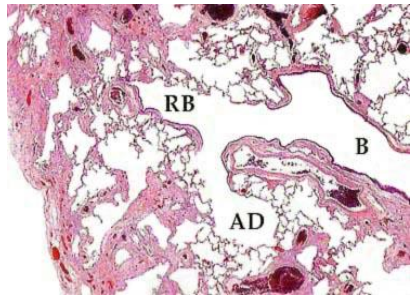
NSIP :

Non specific interstitial pneumonitis

**Immunomodulators? ⟷ Fibromodulators?**

- Systemic scleroderma
- RA, Sjögren
- MCTD
- HSP

…

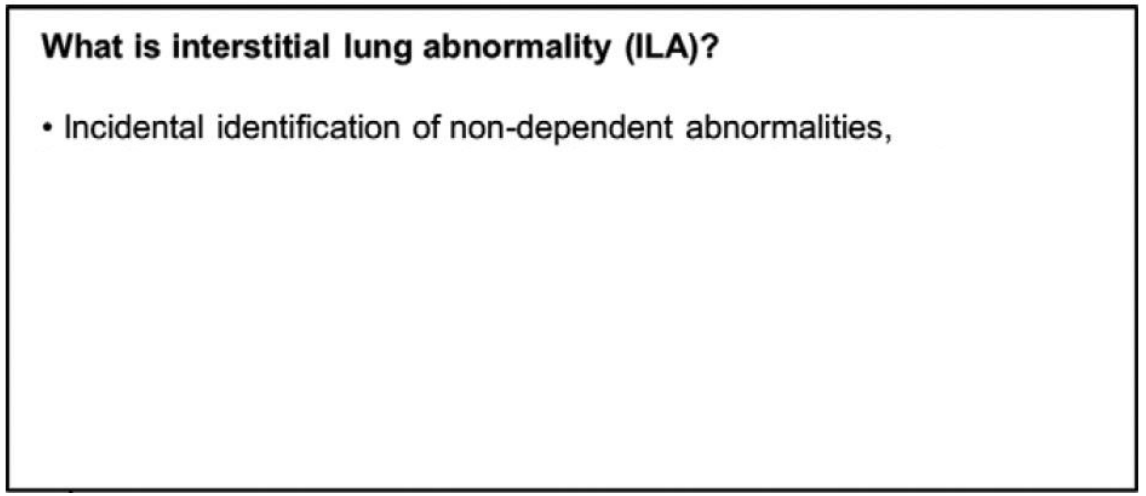



UIP :

Usual interstitial pneumonia

# Définition de l'ILA… (1)

i) **Incidental**
ii) Procubitus CT




*Hata A, Radiology 2021, 301:19*