ILD e artrite reumatoide: un elemento significativo di morbidità e mortalità

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Part of the respiratory tract affected	Clinical manifestation
Airways	Bronchiectasis
	Bronchiolitis
	COPD/emphysema
Pleura	Pleural effusion / pleuritis
Parenchyma	Interstitial lung disease (UIP, NSIP, COP)
	Rheumatoid nodules
	Fibrosis
	Drug-induced pneumonitis (synthetic, biologic DMARDs)
	Infections (pneumonitis), malignancies (lung cancer, lymphoma)
	Emphysema
Vasculature	Vasculitis
	Pulmonary hypertension
	Venous thromboembolism

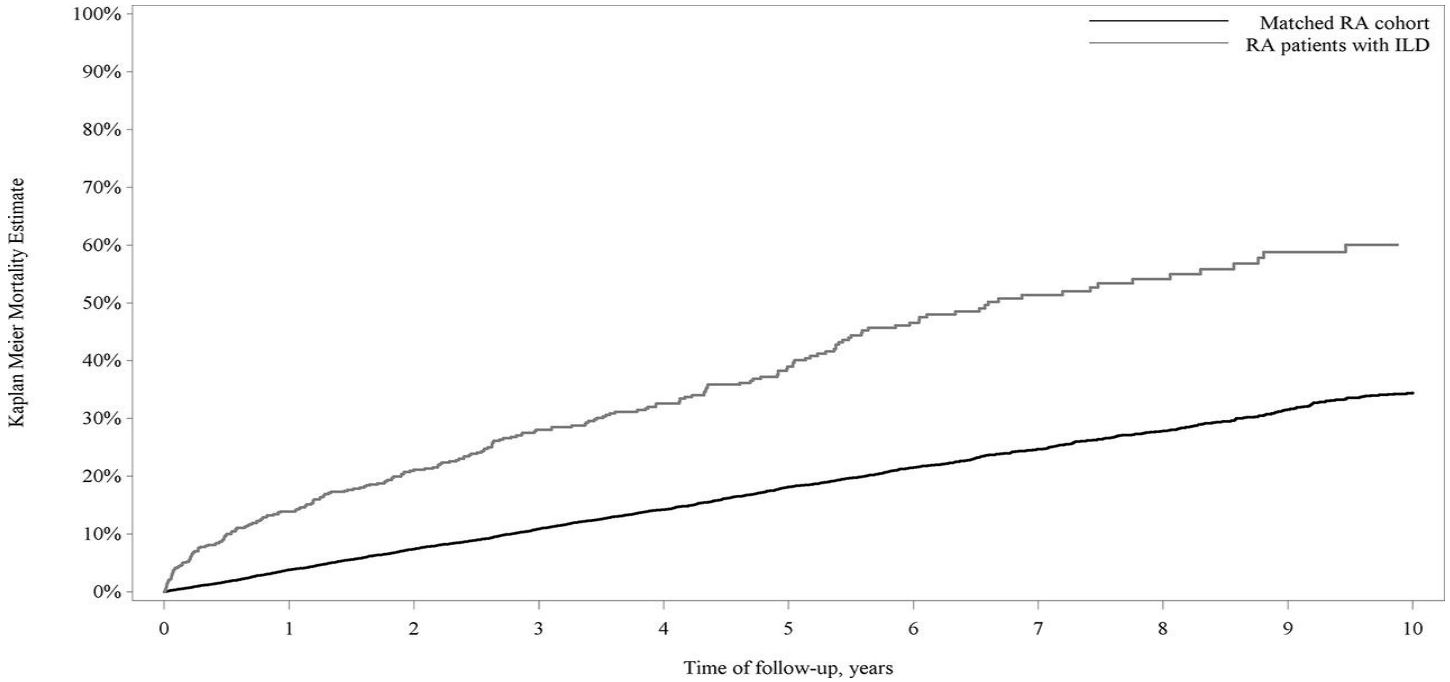
The lung in rheumatoid arthritis, cause or consequence?

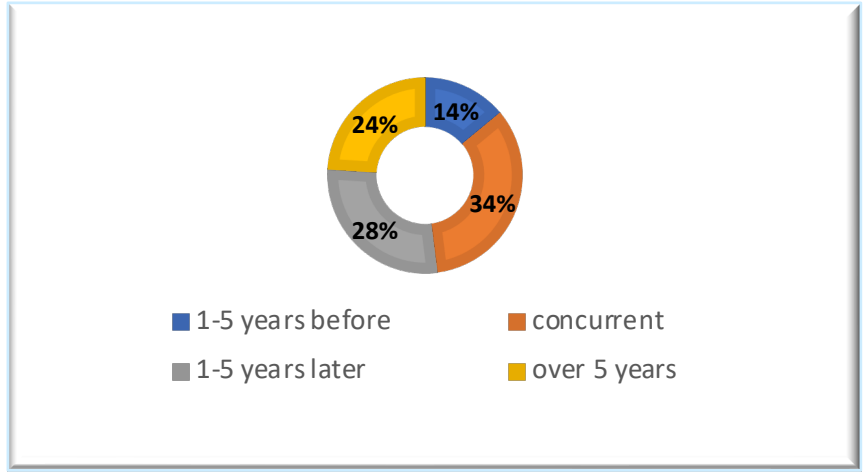
Aikaterini Chatzidionisyou and Anca I. Catrina

Lung is clinically involved in at least 10% of patients, but autoptical studies showed signs of pulmonary involvement in more than 70% of cases

Chatzidionisyou and Anca, Curr Opin Rheumatol 2016, 28:76–82

ILD significantly reduces survival in RA patients





Mortality	ILD	Non-ILD
	%+95% CI	%+95% CI
1-year	**13.9%** (11.4-16.7)	**3.8%** (3.5-4.2)
5-year	**39.0%** (34.4-43.5)	**18.2%** (17.3-19.1)
10-year	**60.1%** (52.9-66.5)	**34.5%** (32.8-36.1)

Hyldgaard C, et al. Ann Rheum Dis. 2017;76:1700-6

HRR for risk of death among RA patients with ILD compared with matched RA cohort

Time of follow-up	Matched RA comparisons, n deaths	Matched RA comparisons, n at risk				
0 to 30 days	41	11 722				
>30 days to 6 months	162	11 577				
>6 months to 1 year	214	10 831	24	572	2.1 (1.4 to 3.3)	1.9 (1.2 to 3.0)
>1 year to 5 years	1055	9707	107	500	2.3 (1.9 to 2.8)	2.0 (1.7 to 2.5)
>5 to 10 years	437	3944	38	170	2.9 (2.0 to 4.1)	2.7 (1.9 to 3.9)

Time of follow-up	Crude HRR (95% CI)	Adjusted HRR (95% CI)*
0 to 30 days	10.0 (6.0 to 16.5)	10.4 (5.9 to 18.2)

- *Adjustment made for seropositivity and Charlson Comorbidity Index.
- HRR, hazard rate ratio; ILD, interstitial lung disease; RA, rheumatoid arthritis.

In stratified analyses, HRR for early death was even higher in males and higher in the age group 65 to 74 years. Seropositivity was not associated with differences in survival when compared with seronegativity/other RA

Hyldgaard C, et al. Ann Rheum Dis. 2017;76:1700-6

Acute exacerbation of interstitial lung disease associated with rheumatic disease

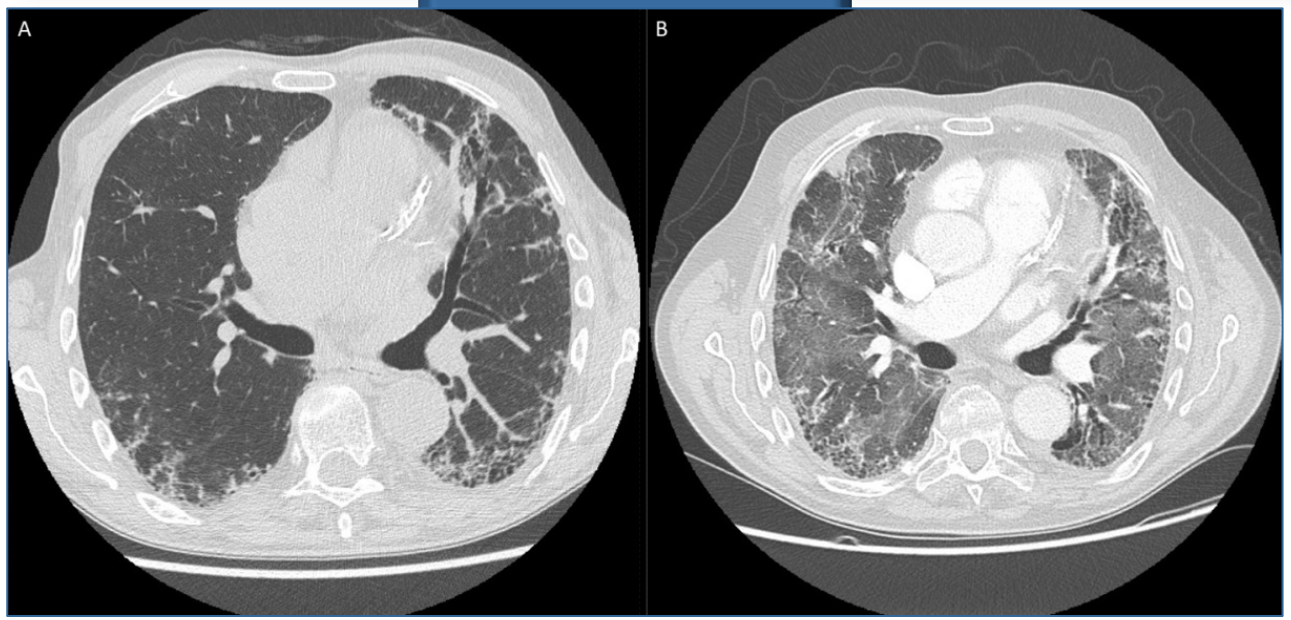
Fabrizio Luppi[1] ✉, Marco Sebastiani[2], Carlo Salvarani[2,3], Elisabeth Bendstrup[4] and Andreina Manfredi[2]

Acute exacerbation: An acute, clinically significant respiratory worsening characterized by new widespread alveolar abnormality in a patient with a known or concurrent diagnosis of rheumatic disease superimposed on a background pattern of ILD. It can be triggered by infections, surgical procedures, DMARDs

A diffuse alveolar damage superimposed to background pattern is the typical histologic picture

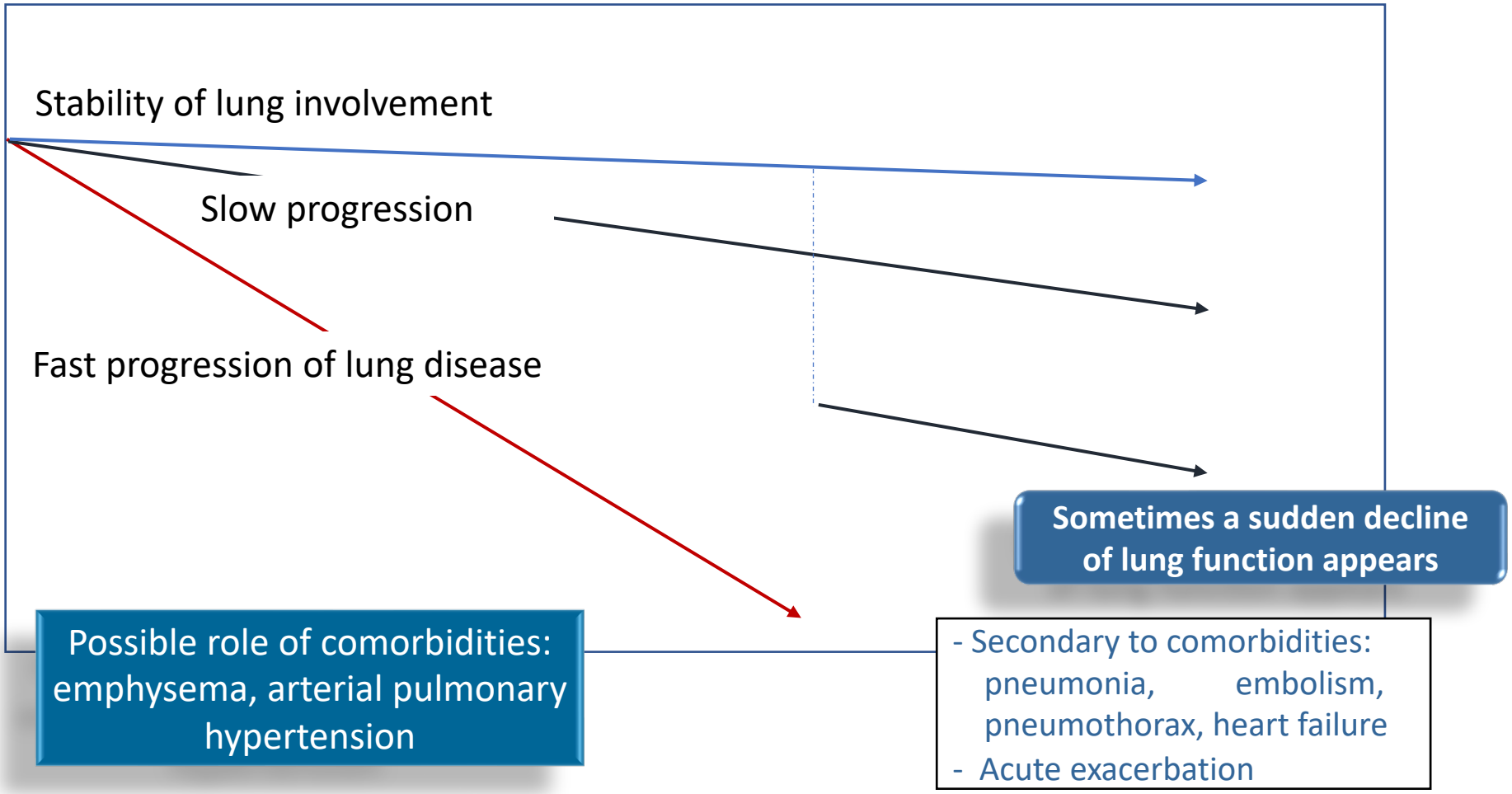
Incidence: 5.77 AE/100 pts/year

Mortality: >50% within 3 months



Luppi F, et al. Nature Rev Rheum, 2021

Unpredictable clinical evolution



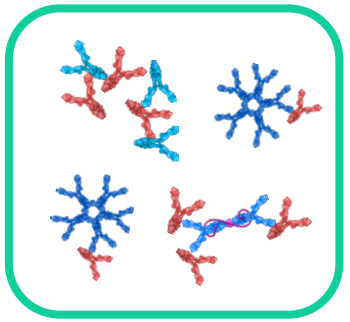
Manfredi A, et al. Expert Rev Clin Immunol. 2021;17:485-97

Risk factors for RA-ILD

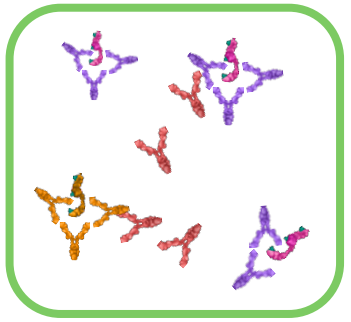
Older Age[1,2]

Male Sex[1,3]

History of ever smoking[3-5]



Seropositivity to RF[4-6]



Seropositivity to ACPA[4-6]

1. Bongartz T, et al. *Arthritis Rheum*. 2010 Jun;62(6):1583-91. 2. Koduri G, *Rheumatology* (Oxford). 2010 Aug;49(8):1483-9. 3. Saag KG, et al. *Arthritis Rheum*. 1996 Oct;39(10):1711-9. 4. Gochuico BR, et al. *Arch Intern Med*. 2008 Jan 28;168(2):159-66. 5. Kelly CA, et al. *Rheumatology* (Oxford). 2014 Sep;53(9):1676-82. 6. Doyle TJ, *Am J Respir Crit Care Med* 2015; 191:1403-1412.

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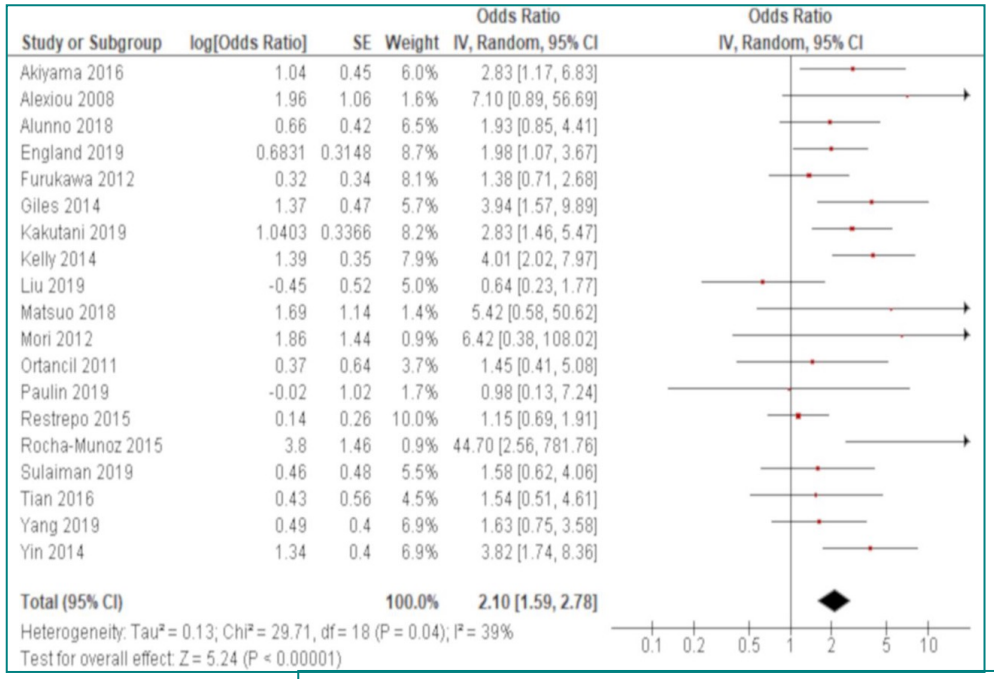
Systematic review and meta-analysis of the risk of rheumatoid arthritis-associated interstitial lung disease related to anti-cyclic citrullinated peptide (CCP) antibody

Hiroyuki Kamiya ,[1] Ogee Mer Panlaqui[2]

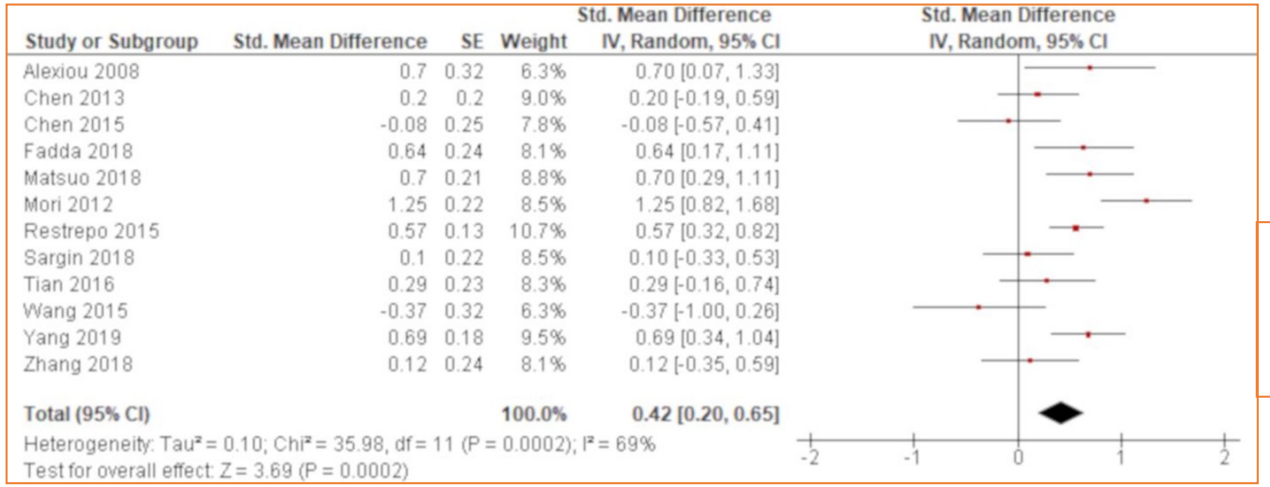
A total of 29 reports were considered for the review



The number of subjects enrolled in each study ranged from 41 to 2702, which amounted to 10158 subjects in total and the mean age at inclusion was between 45.8 and 63.9 years.

All studies except for two contained high risk of bias rating in at least one domain and thus was deemed as high risk of bias

The positivity of anti-CCP antibody was significantly associated with RA-ILD with an OR of 2.10 (95% CI: 1.59 to 2.78). There was moderate heterogeneity



The titre of anti- CCP antibody was significantly higher for RA-ILD than RA without ILD with a standardised mean difference of 0.42 (95% CI: 0.20 to 0.65). There was considerable heterogeneity

Kamiya H, et al. BMJ Open. 2021;11:e040465

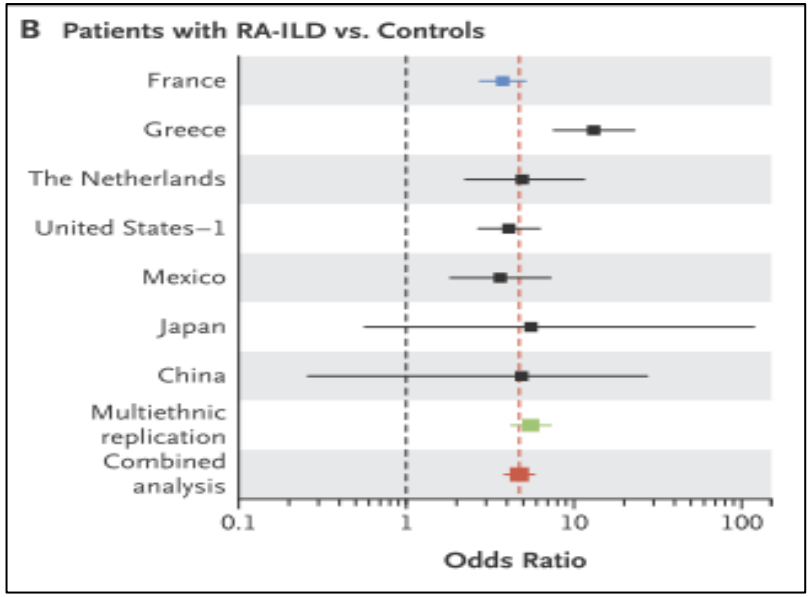
The NEW ENGLAND JOURNAL of MEDICINE

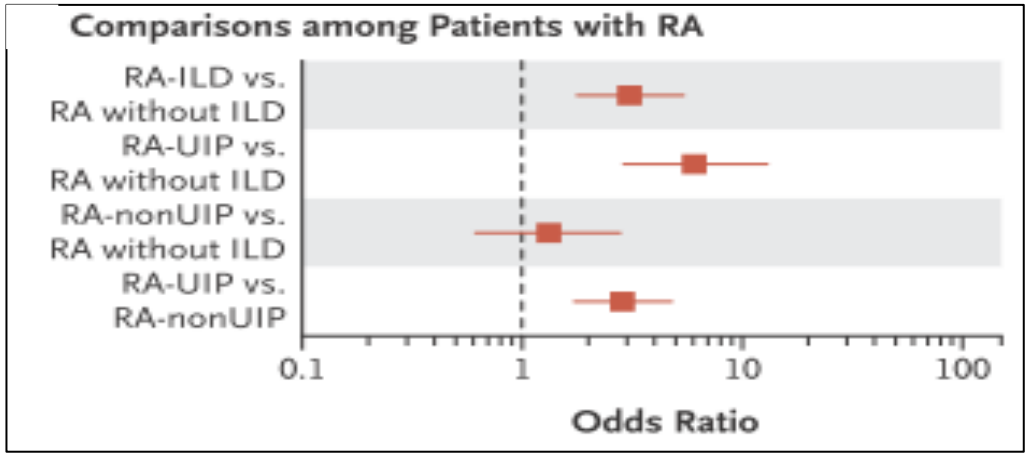
ORIGINAL ARTICLE

MUC5B Promoter Variant and Rheumatoid Arthritis with Interstitial Lung Disease

P.-A. Juge, J.S. Lee, E. Ebstein, H. Furukawa, E. Dobrinskikh, S. Gazal, C. Kannengiesser, S. Ottaviani, S. Oka, S. Tohma, N. Tsuchiya, J. Rojas-Serrano, M.I. González-Pérez, M. Mejía, I. Buendía-Roldán, R. Falfán-Valencia, E. Ambrocio-Ortiz, E. Manali, S.A. Papiris, T. Karageorgas, D. Boumpas, K. Antoniou, C.H.M. van Moorsel, J. van der Vis, Y.A. de Man, J.C. Grutters, Y. Wang, R. Borie, L. Wemeau-Stervinou, B. Wallaert, R.-M. Flipo, H. Nunes, D. Valeyre, N. Saidenberg-Kermanac'h, M.-C. Boissier, S. Marchand-Adam, A. Frazier, P. Richette, Y. Allanore, J. Sibilia, C. Dromer, C. Richez, T. Schaeverbeke, H. Lioté, G. Thabut, N. Nathan, S. Amselem, M. Soubrier, V. Cottin, A. Clément, K. Deane, A.D. Walts, T. Fingerlin, A. Fischer, J.H. Ryu, E.L. Matteson, T.B. Niewold, D. Assayag, A. Gross, P. Wolters, M.I. Schwarz, M. Holers, J. Solomon, T. Doyle, I.O. Rosas, C. Blauwendraat, M.A. Nalls, M.-P. Debray, C. Boileau, B. Crestani, D.A. Schwartz, and P. Dieudé

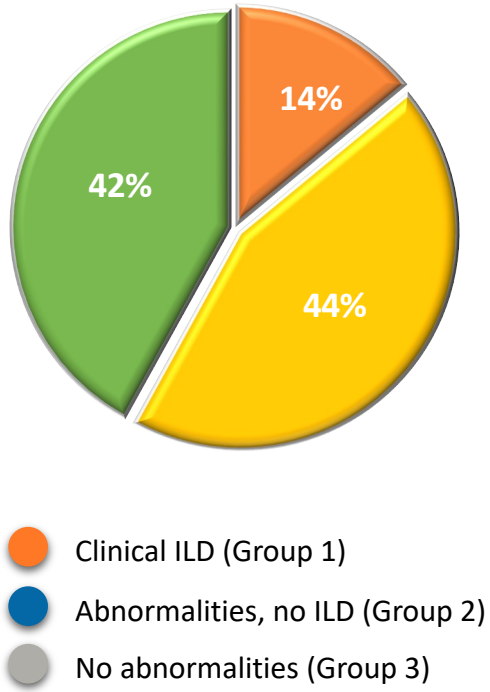
The common gain-of-function variant rs35705950 in the promoter of MUC5B, encoding mucin 5B, is the strongest genetic risk factor for idiopathic pulmonary fibrosis. it is observed in at least 50% of patients with IPF and accounts for 30% of the risk of developing this disease.





The MUC5B promoter variant may prove to be a generalized risk factor for UIP disease and not simply limited to IPF and RA-ILD. In fact, emerging studies have identified the MUC5B promoter variant as a risk factor for chronic hypersensitivity pneumonitis, another condition known to have a sub-phenotype of a UIP pattern

Is there any evidence for HRCT screening in RA?



- 36 patients (25 women and 11 men):
  - 61% (22 of 36) were RF+
  - 83% (30 of 36) treated with DMARDs
  - 58% (21 of 36) treated with methotrexate
- Duration of joint symptoms was < 2 yr
- Patients were classified into three groups according to the presence and type of abnormality as follows:
  - Group 1 - **Clinically significant ILD: 14% of patients (5 out of 36**)
  - Group 2 - **Abnormalities compatible with ILD, but no clinically significant ILD: 44% of patients (16 out of 36) (HRCT or PFT or BAL)**
  - Group 3 - No abnormalities compatible with ILD: 42% of patients (15 out of 36)

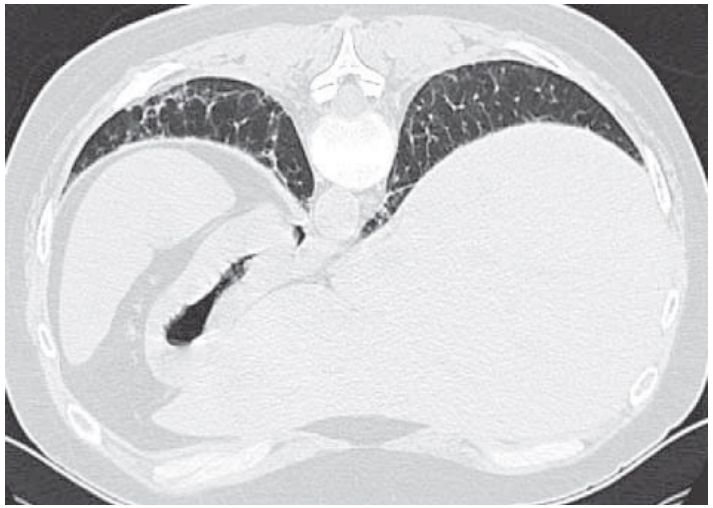
12 (33%) patients had HRCT alterations compatible with ILD

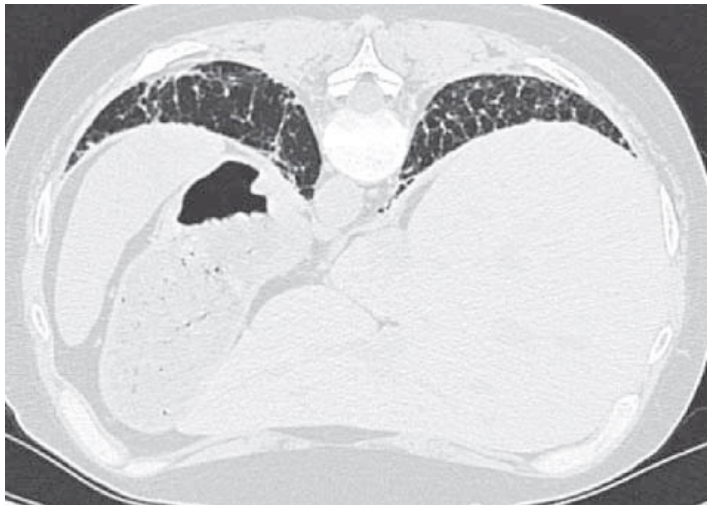
Gabbay E, et al. *Am J Respir Crit Care Med.* 1997;156:528-35

Is there any evidence for HRCT screening in RA?

Preclinical HRCT alterations:

- Long standing RA patients (disease duration 12 years)
- 21/64 (33%) patients without dyspnea or cough had features of “preclinical” ILD at HRCT
- A progression of ILD at HRCT has been observed in 12/21 (57%)





Gochuico et al *Arch Intern Med* 2008

Is there any alternative to HRCT screening in RA-ILD?

150 consecutive RA patients

Clinical evaluation, HRCT and thorax X-Ray within 4 weeks by spirometry and DLCO

28/150 (19%) patients with ILD at HRCT

	Fibrosing alveolitis	**No fibrosing alveolitis**	***p***
Bibasal velcro-crackles	54%	9%	**<0.001**
Reduction of Dlco <75% predicted	82%	52%	**0.006**
Restrictive syndrome at spirometry	14%	4%	0.06
X-Ray signs	14%	5%	0.09
Dyspnoea: NYHA grade II	54%	56%	0.84
Dyspnoea: NYHA grade III	18%	6.5%	0.07

Dawson JK et al. *Thorax* 2001;56:622-7

Neglected evidence in idiopathic pulmonary fibrosis and the importance of early diagnosis and treatment

Vincent Cottin[1,2] and Luca Richeldi[3,4]

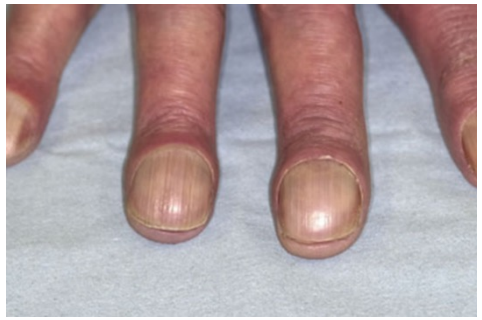
Diagnosis of RA-ILD is often late or absent, with possible severe prognostic implications.

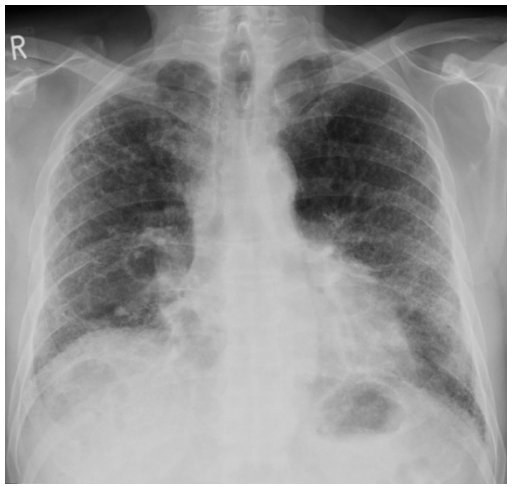
An early diagnosis presupposes availability of easily repeatable diagnostic tools, at low cost, which can also be performed in first and second level centers and without exposure of the patient to ionizing radiation

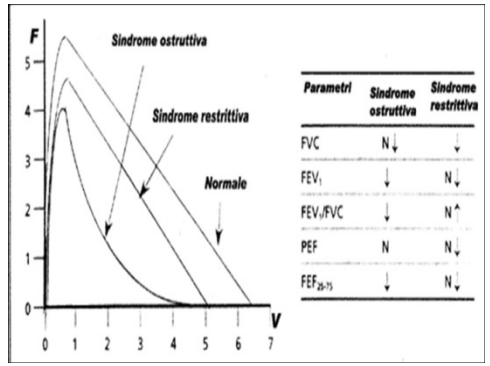
Eur Respir Rev. 2014;23:106-10

Diagnostic accuracy of clinical and instrumental variables

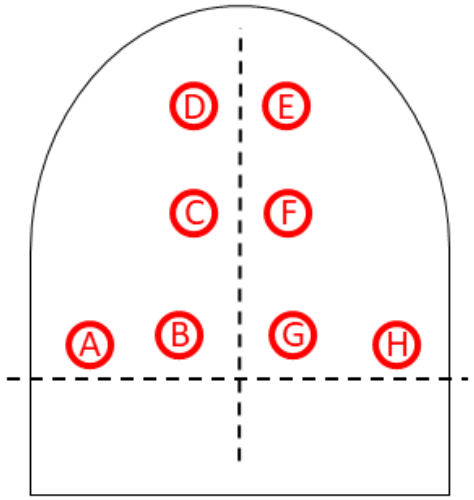
	Total	diagnostic accuracy	specificity	sensitivity
Dyspnoea	29.1	64.6	81.3	41.8
Dry cough	12.1	58.3	89.2	15.1
Thorax X-Ray	35.1	71.3	80	57.8
DLCO < 47	26	54.9	80	30.8
Velcro crackles	49.2	67.2	65.7	69.1
Velcro crackles		**83.9**	**76.9**	**93.2**





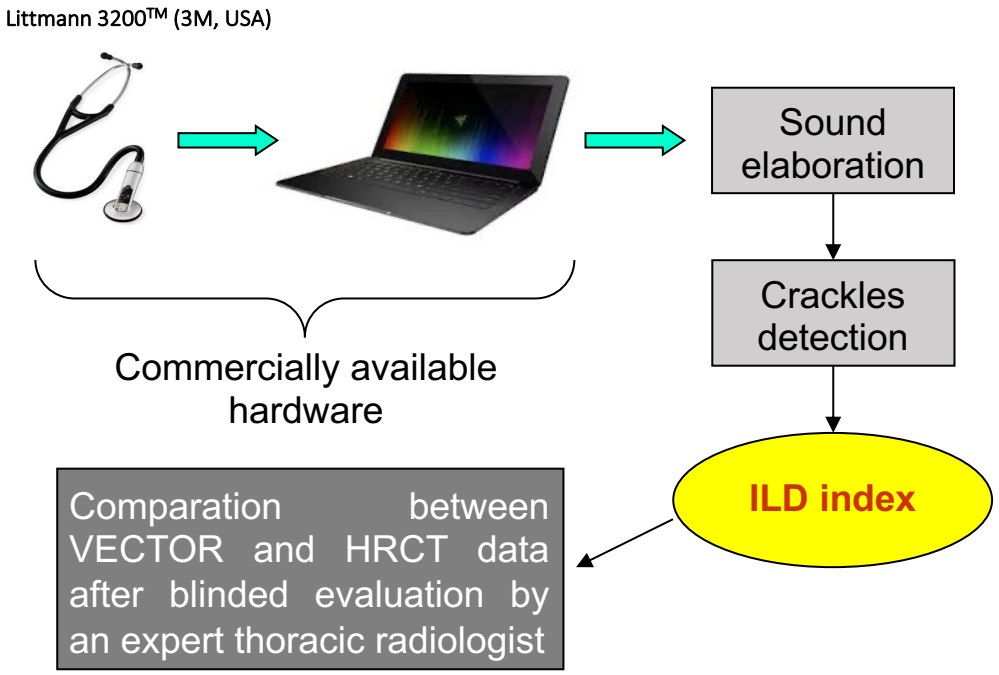


Manfredi et al. BMC Pulmonary Medicine. 2019;19:111



All consecutive RA patients, that have been performed HRCT within 12 months, in the absence of the subsequent appearance or variation of signs or symptoms suggestive of lung disease, were included in the study.
The reason for HRCT prescription was not a selection criterion for participation in the study.

Respiratory sounds were recorded in 4 pulmonary fields bilaterally (2 at the basal field, 1 at the middle field and 1 at the upper field) in a silent environment with a commercial ES (Littmann 3200™ 3 M, USA). Then, audio files acquired for each patient were digitized, coded, saved as a WAV file and analyzed by mean of VECTOR.



RESEARCH ARTICLE Open Access

"Velcro-type" crackles predict specific radiologic features of fibrotic interstitial lung disease

The presence of pulmonary fibrosis was strongly associated with "Velcro-type" crackles.
Multivariate analysis of radiologic features identified that reticulation, honeycombing, ground glass opacities and traction bronchiectasis were all independently associated with the presence of "Velcro-type" crackles in the lung parenchyma underneath

Table 3 Univariate (A) and multivariate (B) logistic regression of individual radiologic features on HRCT sections toward presence of "Velcro-type" crackles on corresponding recording sites. Data presented as odds ratios (OR) with 95% confidence intervals (CI) and *p* value

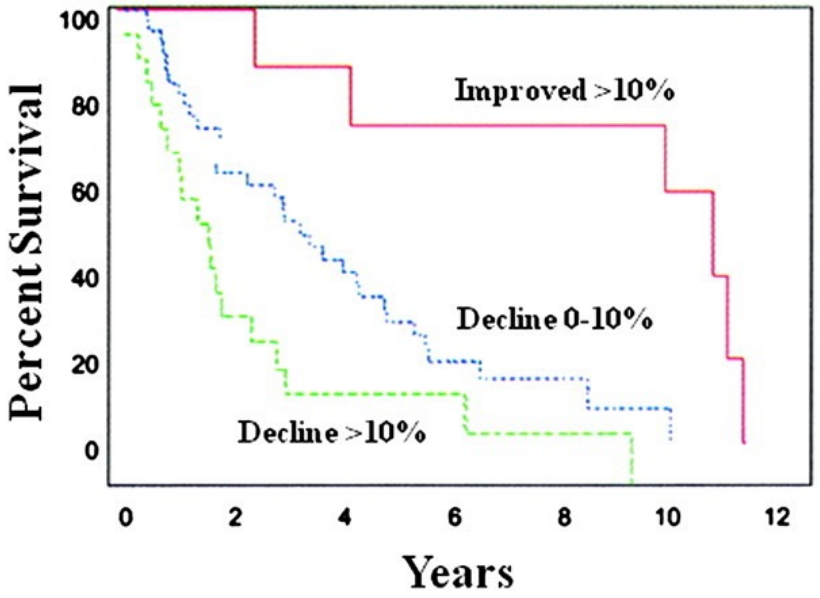
Feature	OR (95% CI)	*p* value
A		
Fibrosis	6.24 (4.5–8-66)	< 0.001
Ground glass opacities	2.13 (1.61–2.81)	< 0.001
Reticulation	2.57 (2.14–3.09)	< 0.001
Traction bronchiectasis	4.37 (3.17–6.02)	< 0.001
Honeycombing	2.39 (1.52–3.76)	< 0.001
Emphysema	0.72 (0.5–1.04)	0.077
B		
Ground glass opacities	1.74 (1.29–2.32)	< 0.001
Reticulation	2.04 (1.62–2.57)	< 0.001
Traction bronchiectasis	1.55 (1.03–2.32)	< 0.05
Honeycombing	1.88 (1.24–2.83)	< 0.01

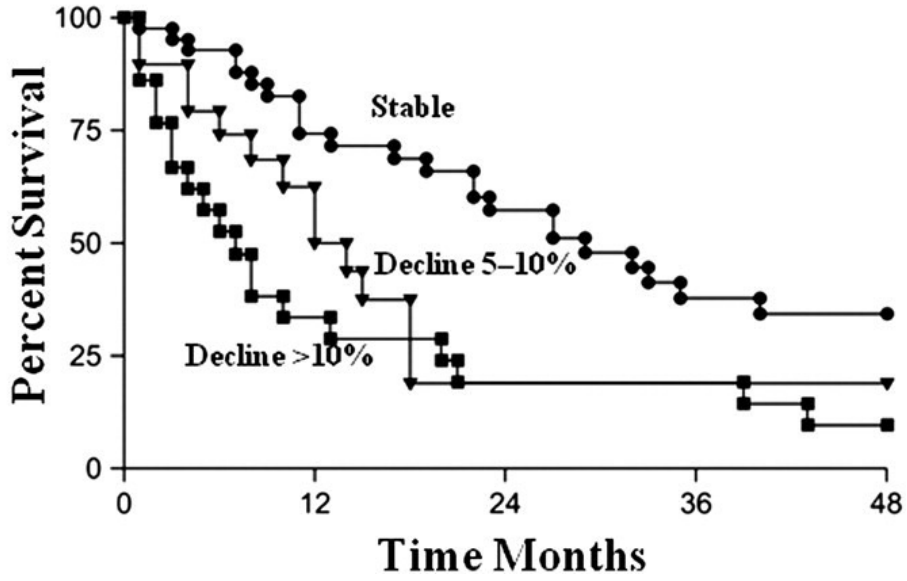
Table 2 Relationships between presence of unilateral or bilateral "Velcro-type" crackles and radiologic pattern on HRCT. Data expressed as Odds ratio (OR) with 95% Confidence Intervals (95% CI) and *p* value

HRCT pattern	Bilateral "Velcro-type" crackles		Unilateral "Velcro-type" crackles	
	OR (CI 95%)	*p*	OR (CI 95%)	*p*
FILD	13.46 (5.71–29.182)	< 0.001	0.58 (0.29–1.16)	0.12
Definite UIP	19.8 (5.28–74.25)	< 0.001	0.49 (0.14–1.66)	0.25
Possible UIP	13.09 (4.87–35.2)	< 0.001	0.55 (0.23–1.34)	0.19
Inconsistent with UIP	10.8 (3.85–32.85)	< 0.001	0.75 (0.26–2)	0.53

FVC decline predicts survival in IPF

Survival in relation to the magnitude of change in FVC at 6 months.





Collard HR, et al. *Am J Respir Crit Care Med* 2003;168:538–42

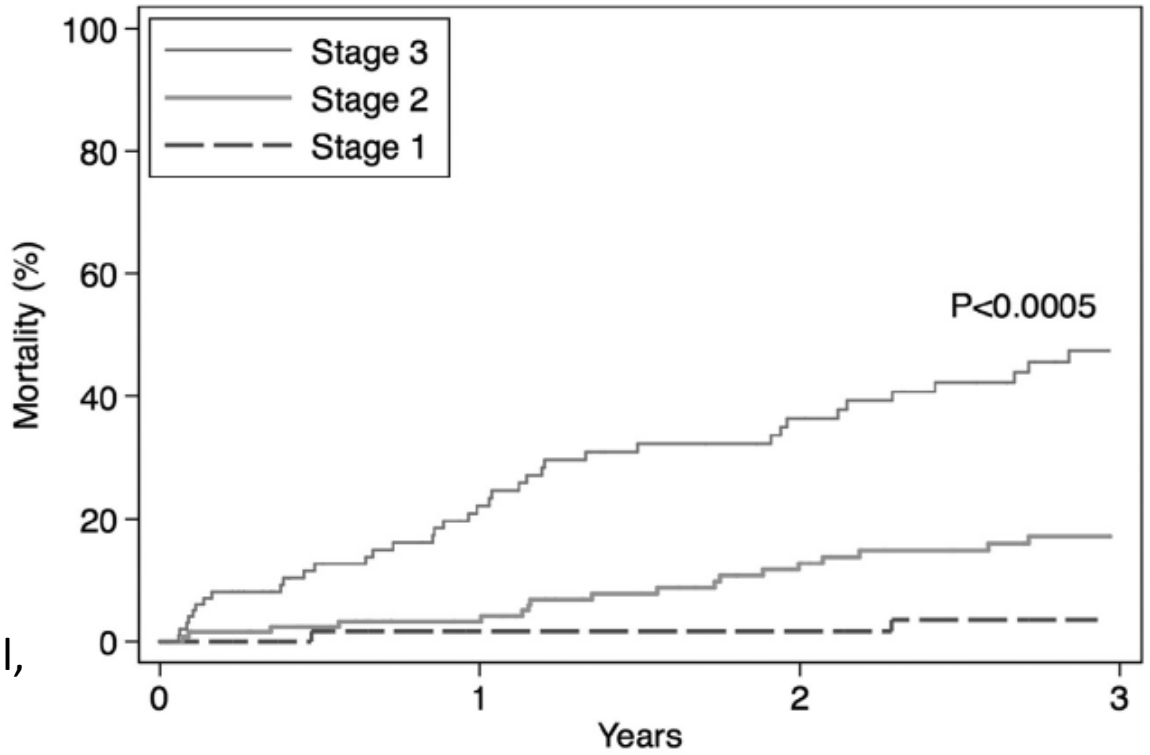
Zappala CJ, et al. Eur Respir J 2010;35:830–6

The performance of the GAP model in patients with rheumatoid arthritis associated interstitial lung disease

Julie Morisset, M.D.[1], Eric Vittinghoff, Ph.D.[2], Bo Young Lee, M.D.[3], Roberto Tonelli, M.D.[4], Xiaowen Hu, M.D.[5], Brett M Elicker, M.D.[6], Jay H Ryu, M.D.[5], Kirk D Jones, M.D.[7], Stefania Cerri, M.D.[4], Andreina Manfredi, M.D.[8], Marco Sebastiani, M.D.[8], Andrew J Gross, M.D.[1], Brett Ley, M.D.[1], Paul J Wolters, M.D.[1], Talmadge E King Jr., M.D.[1], Dong Soon Kim, M.D.[3], Harold R Collard, M.D.[1], and Joyce S Le, M.D.[9]

	Predictor	Points
G	Gender	
	Female	0
	Male	1
A	Age, y	
	≤60	0
	61–65	1
	>65	2
P	Physiology	
	FVC, *% predicted*	
	>75	0
	50–75	1
	<50	2
	DLCO, *% predicted*	
	>55	0
	36–55	1
	≤35	2
	Cannot perform	3
	Total Possible Points	8

Stage	I	II	III
Points	0–3	4–5	6–8
Mortality			
1-y	5.6	16.2	39.2
2-y	10.9	29.9	62.1
3-y	16.3	42.1	76.8



Retrospective study, four centers (Mayo Clinic Rochester, Seoul, UCSF, AOU di Modena)

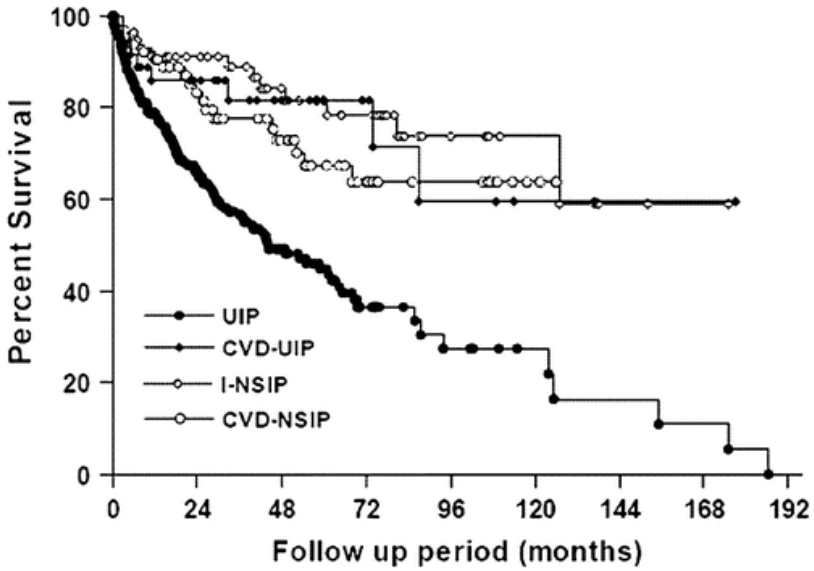
Final cohort : 309 patients with RA-ILD

Morisset J et al *Resp Med* 2017; 127:51-56

Radiologic ILD pattern is a major prognostic factor in RA patients

Prognosis of Fibrotic Interstitial Pneumonia
Idiopathic versus Collagen Vascular Disease–related Subtypes

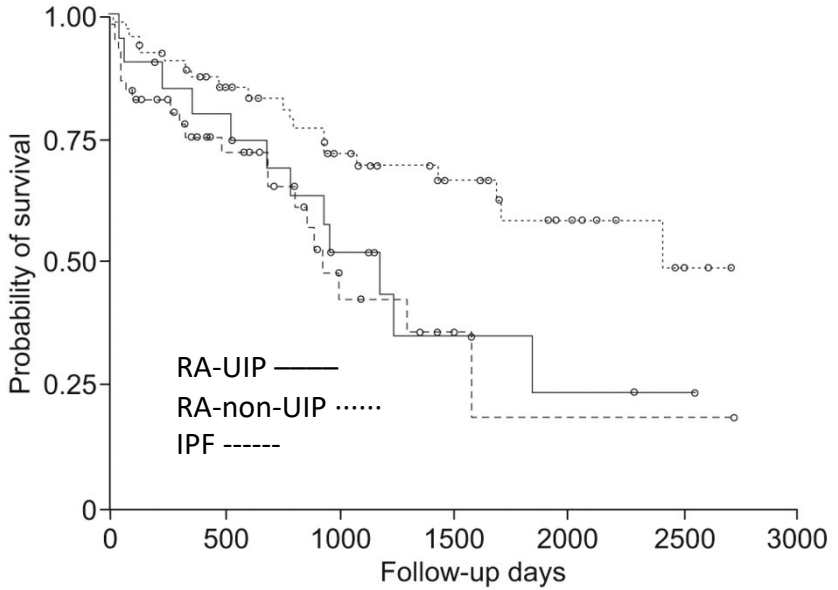
Joo Hun Park[1], Dong Soon Kim[1], I-Nae Park[1], Se Jin Jang[2], Masanori Kitaichi[3], Andrew G. Nicholson[4], and Thomas V. Colby[5]



Park JH, et al. Am J Respir Crit Care Med. 2007;175:705-11

Usual interstitial pneumonia in rheumatoid arthritis-associated interstitial lung disease

E.J. Kim*, B.M. Elicker#, F. Maldonado¶, W.R. Webb#, J.H. Ryu¶, J.H. Van Uden#, J.S. Lee*, T.E. King Jr* and H.R. Collard*



E. J. Kim et al. Eur Respir J 2010;35:1322-1328

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

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

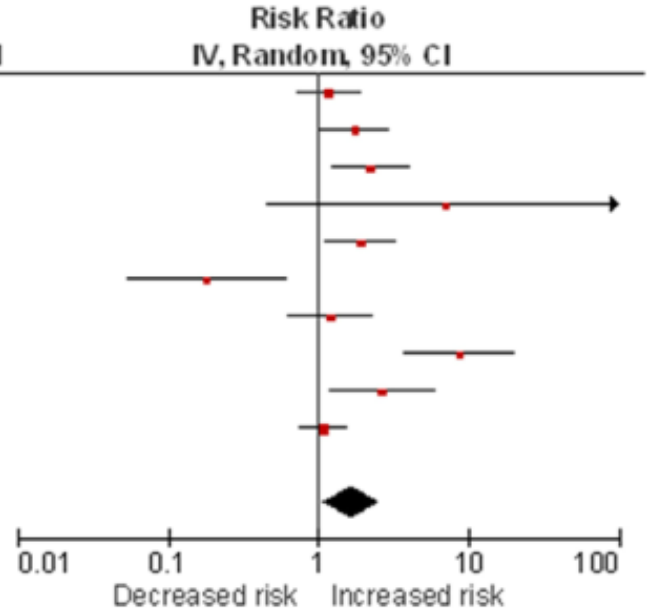
Impact of the pattern of interstitial lung disease on mortality in rheumatoid arthritis: A systematic literature review and meta-analysis

Namrata Singh[a,*], Jimmy Varghese[a], Bryant R. England[b], Joshua J. Solomon[c], Kaleb Michaud[b,d], Ted R. Mikuls[b], Heather S. Healy[e], Emily M. Kimpston[f], Marin L. Schweizer[g]

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Fu	0.14842	0.25510336	12.3%	1.16 [0.70, 1.91]
Hozumi	0.553885	0.27573359	12.0%	1.74 [1.01, 2.99]
Jacob	0.79299252	0.31096554	11.4%	2.21 [1.20, 4.07]
Lee	1.94591	1.395726	2.2%	7.00 [0.45, 107.93]
Nurmi	0.650588	0.285784	11.8%	1.92 [1.09, 3.36]
Rojas-Serrano	-1.71479843	0.62265611	6.8%	0.18 [0.05, 0.61]
Solomon	0.182322	0.32886249	11.1%	1.20 [0.63, 2.29]
Tsuchiya	2.15416509	0.42955063	9.5%	8.62 [3.71, 20.01]
Yang	0.97077892	0.41576589	9.7%	2.64 [1.17, 5.96]
Zamora-Legoff	0.08685952	0.19026775	13.3%	1.09 [0.75, 1.58]
Total (95% CI)			**100.0%**	**1.66 [1.07, 2.56]**

Heterogeneity: $Tau^2 = 0.33$; $Chi^2 = 38.05$, df = 9 ($P < 0.0001$); $I^2 = 76\%$

Test for overall effect: $Z = 2.29$ ($P = 0.02$)



Meta-analysis yielded a pooled RR of 1.66 (95% CI 1.07 to 2.56) for death among those with UIP RA-ILD compared with other patterns. In sub-group analysis when pooling studies comparing UIP to NSIP pattern of RA-ILD, the RR was 2.39 (95% CI 0.866.68).

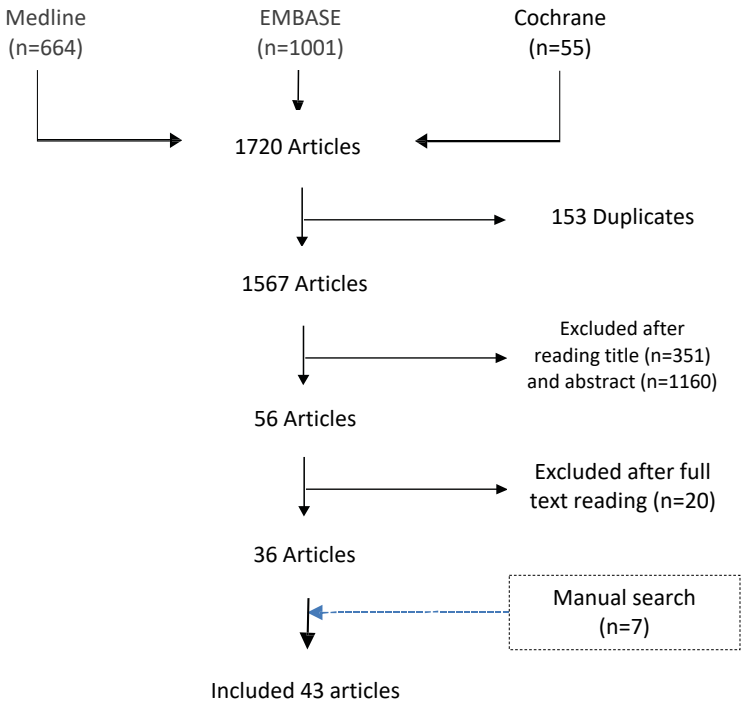
Singh N, et al. Semin Arthritis Rheum. 2019;49:358-65

No agreement about the therapeutic approach to patients with rheumatoid arthritis and ILD

- No correlation between joint and lung disease activities
- No evidence that treatment of joint involvement is effective on lung involvement
- Immunosuppressants usually prescribed for the treatment of ILD related to CTDs are not effective on arthritis
- Many DMARDs used in rheumatoid arthritis have been demonstrated possible toxicitiy on the lung

Manfredi A, et al. Expert Rev Clin Immunol. 2021;17:485-97

Systematic review of studies evaluating the impact of pharmacological treatment in patients with RA and ILD



No evidence that **MTX** or **LEF** worsens the prognosis of patients with RA-ILD

RTX and **ABA** show better results than other bDMARDs, such us TNFi, often achieving stabilization and, in some cases, the improvement of ILD in patients with RA

Scarce evidence for JAKi and controversial for IL-6 inhibitors

2019 Update of the British Society for Rheumatology biologic DMARD safety guidelines in inflammatory arthritis

Respiratory disease

i. Pre-existing ILD is **not a specific contraindication** to biologic therapy; however, **caution is advised** in patients with poor respiratory reserve (in whom a significant drop in lung function would be potentially life threatening); in this situation it is advised to work closely with a respiratory physician with a specialist interest in ILD (grade 2C, SOA 99%).

ii. **RTX** or **ABA** may be considered a **first-line biologic** in patients with ILD (grade 2C, SOA 84%).

GUIPCAR 2017

Guidelines for the management of RA in Spain

In patients with RA, which is the safest biological treatment in patients who also have ILD?

Recommendation and degree of recommendation after systematic review of the literature

- In patients with RA and ILD who require biological therapy, it is recommended to use **ABA** as the safest option *(Recommendation grade C)*
- As an alternative, **RTX** can be used *(Recommendation grade D)*

RHEUMATOLOGY
Rheumatology 2017;56:1348–1357
doi:10.1093/rheumatology/kex072
Advance Access publication 24 April 2017

Original article

Effect of rituximab on the progression of rheumatoid arthritis–related interstitial lung disease: 10 years' experience at a single centre

Md Yuzaiful Md Yusof[1,2], Angela Kabia[1], Michael Darby[3], Giovanni Lettieri[1], Paul Beirne[4], Edward M. Vital[1,2], Shouvik Dass[1,2] and Paul Emery[1,2]

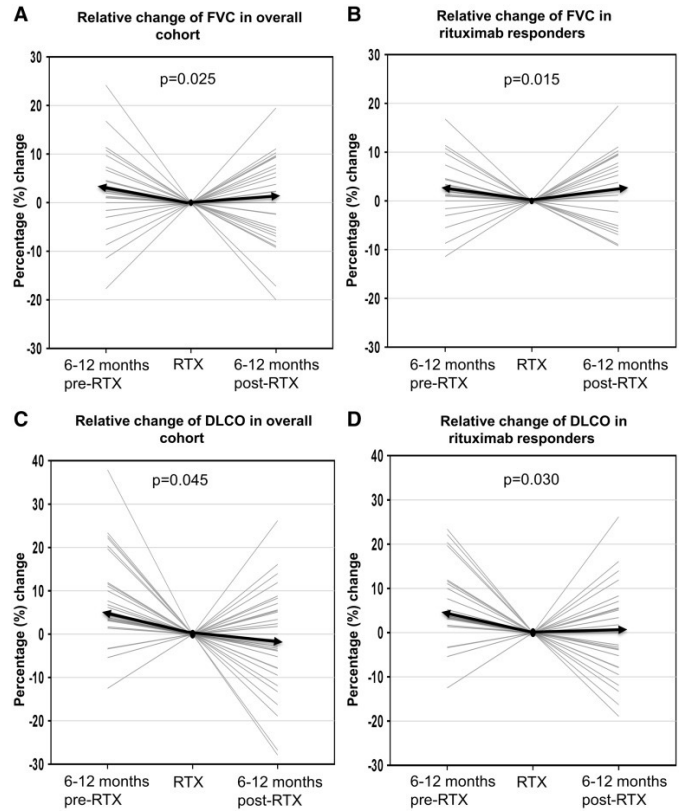
56 patients with ILD at baseline, 44 with availability of lung function data before and after therapy, 7 deaths

After RTX treatment

7/44 (16%) defined improved

23/44 (52%) defined stable

14/44 (32%) ILD progression



Letters to the Editors

Interstitial lung disease is associated to infections of lower respiratory tract in immunocompromised rheumatoid arthritis patients

M. SEBASTIANI, *MD*[1]
A. MANFREDI, *MD*[1]
G. CASSONE, *MD*[1]
G. SANDRI, *MD*[1]
S. CERRI, *MD*[2]
C. FERRI, *MD*[1]
[1]*Rheumatology Unit, and* [2]*Respiratory Disease*

and clinical features and LRT infections in this sub-group of patients.
Among 33/563 (5.9%) patients with ILD, diagnosed on the basis of high-resolution computerised tomography (HRCT) (female/male ratio 2/1, mean age 71.8±10.6 years, mean disease duration 16.1±13.0 years),

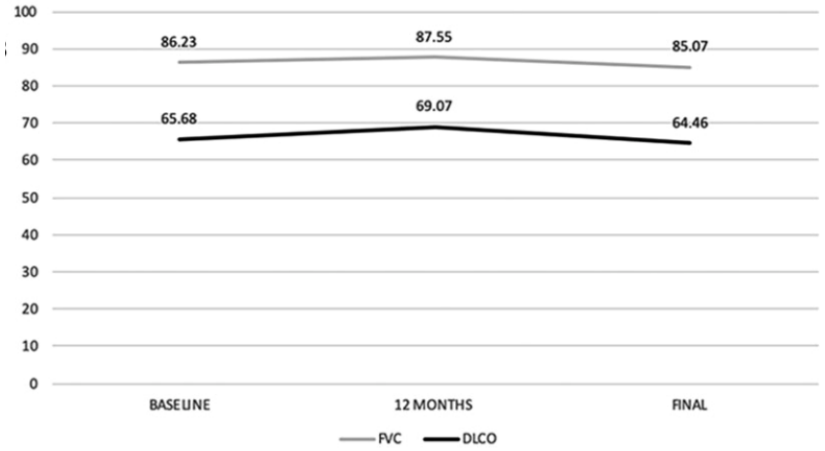
Md Yusof MY, et al. Rheumatology. 2017

RHEUMATOLOGY
Rheumatology 2020;0:1–11
doi:10.1093/rheumatology/keaa621
Original article

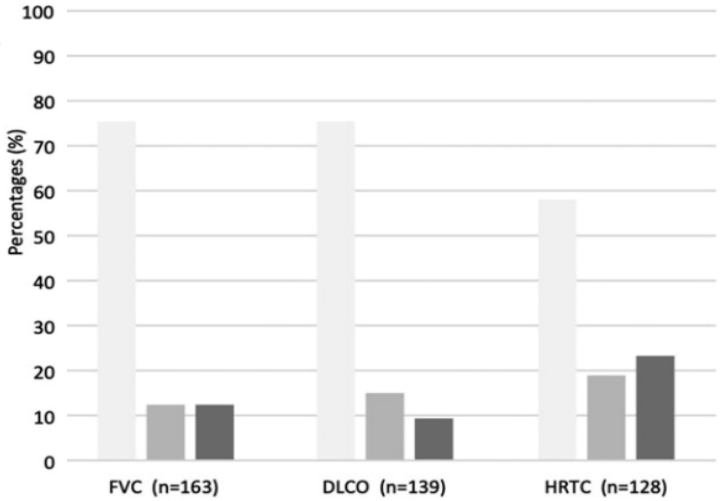
Abatacept in interstitial lung disease associated with rheumatoid arthritis: national multicenter study of 263 patients

It was prescribed as **mono-therapy (n=111, 42.2%)** or combined with the following cDMARDs (n=152): **LFN (n=55)**, **MTX (n=41)**……

ABA was the **first-line therapy in 60 patients** after ILD was diagnosed and the **first biologic therapy in other 142 patients** .



Follow-up 22.66 months (19.66)



Chest HRCT available in 128 patients

- Stability	74 pts (57.8%)
- Improvement	24 pts (18.8%)
- Worsening	30 pts (23.4%)

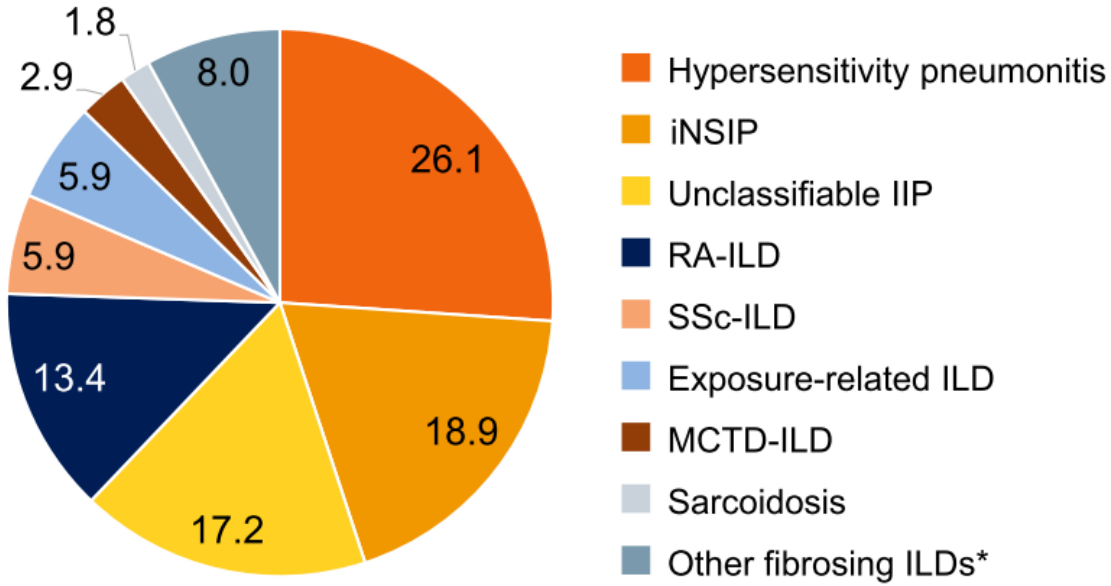
Fernández-Díaz C et al. Rheumatology, 2020

The aim of the INBUILD trial was to evaluate the efficacy and safety of nintedanib in patients with non-IPF chronic fibrosing ILDs with a progressive phenotype

Eligible patients met ≥1 of 4 criteria for ILD progression in the 24 months before screening, despite treatment of ILDs in clinical practice as applicable:

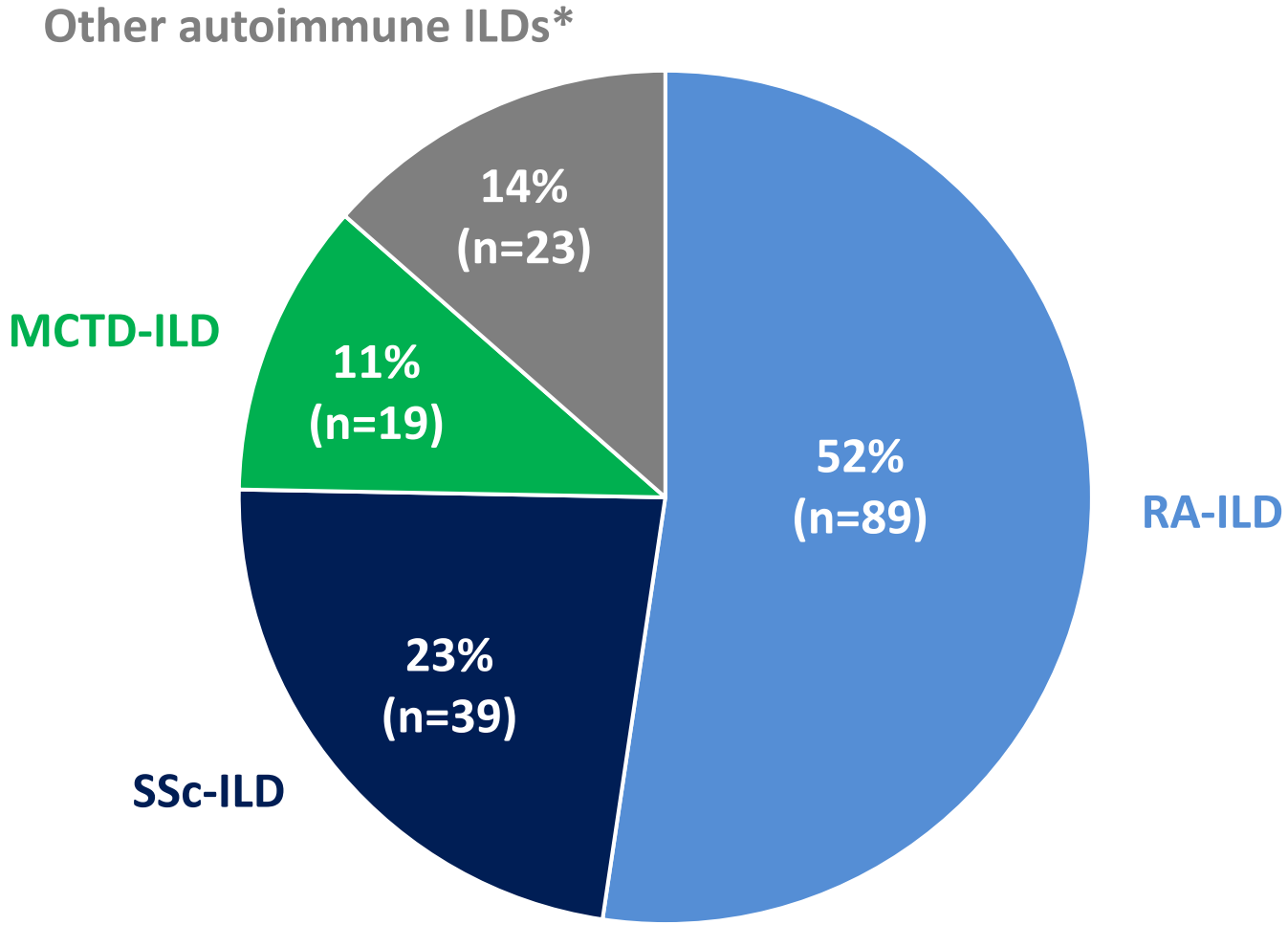
- Relative decline in FVC ≥10% predicted
- Relative decline in FVC ≥5–<10% predicted and worsened respiratory symptoms
- Relative decline in FVC ≥5–<10% predicted and increased extent of fibrotic changes on chest imaging
- Worsened respiratory symptoms and increased extent of fibrotic changes on chest imaging

ILD diagnoses in 9 subgroups by ILD diagnosis



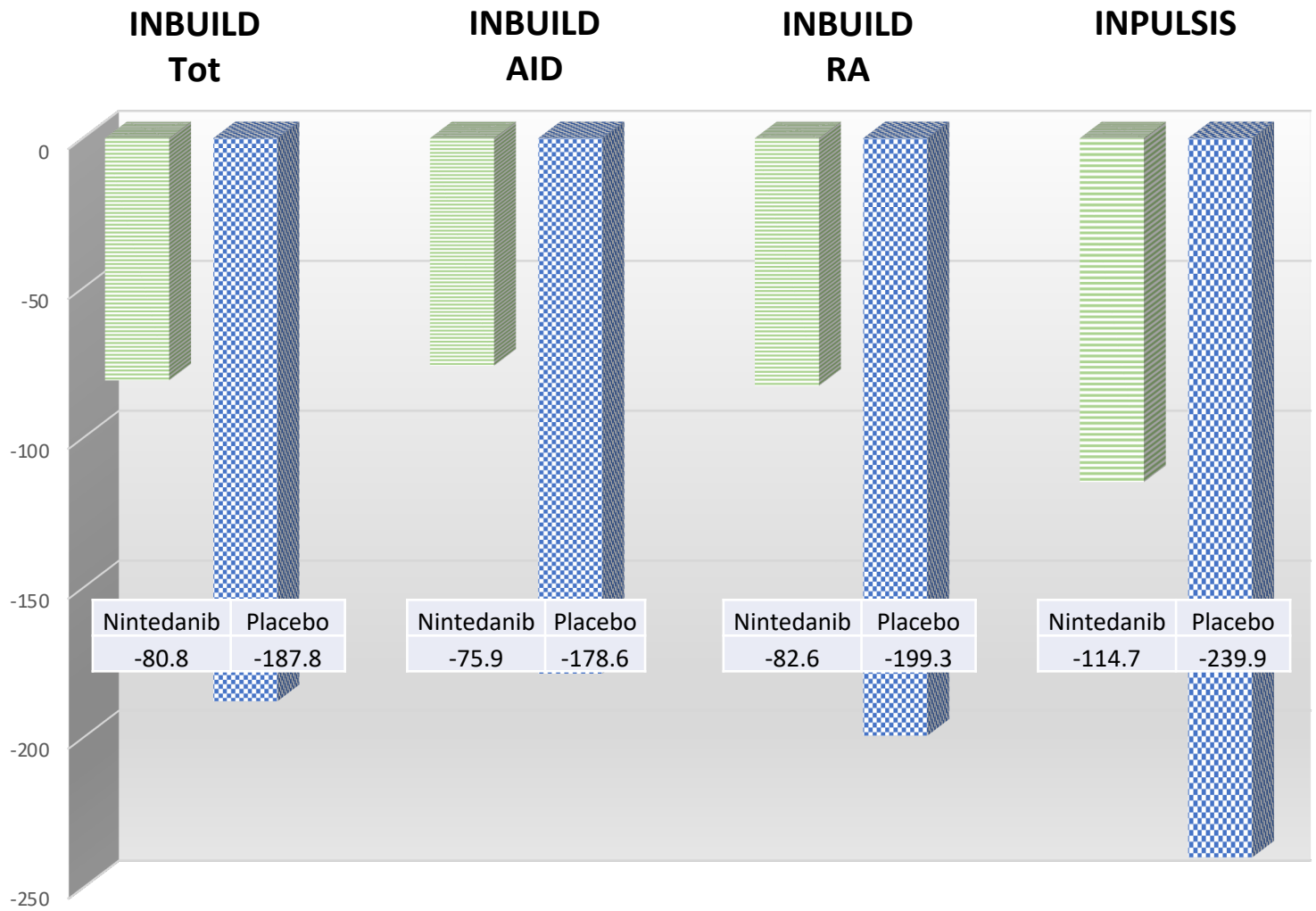
Flaherty KR et al. N Engl J Med 2019;381:1718–27

INBUILD: ILD diagnoses in subjects with autoimmune disease-related ILDs (n=170)



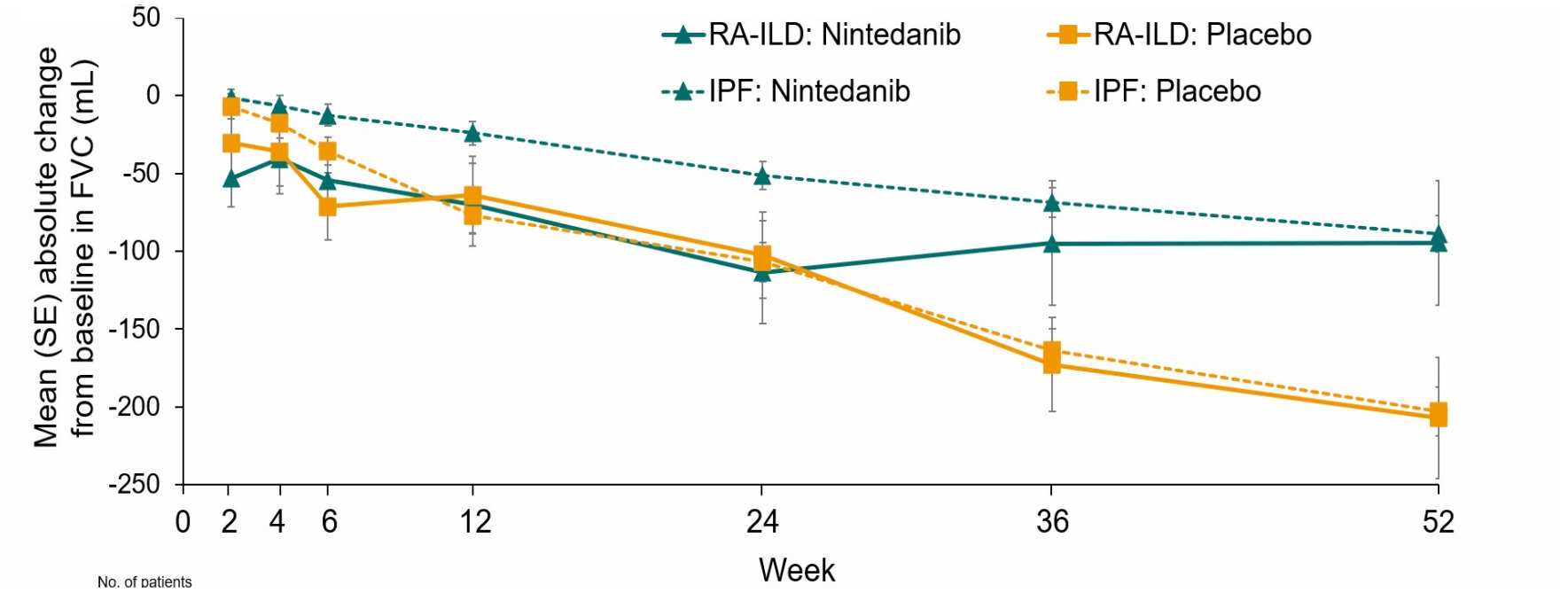
*Subjects with an autoimmune disease noted in the "Other fibrosing ILDs" category of the case report form, including Sjogren's disease-related ILD, IPAF, and undifferentiated autoimmune disease-related ILD.

Decline of FVC in INBUILD subgroups

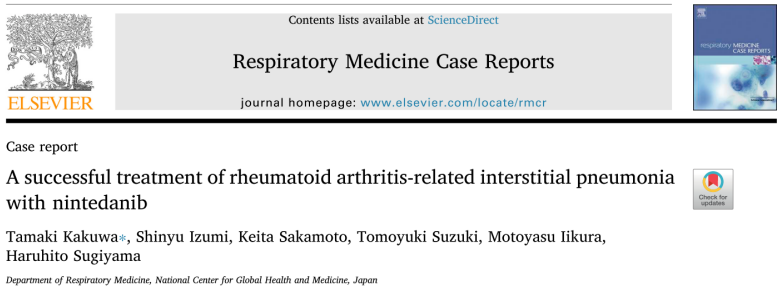


Kelly C et al. Effects of nintedanib in patients with progressive fibrosing RA-ILD in the INBUILD trial. EULAR, 2021

Absolute change in FVC (mL) in patients with RA-ILD in INBULID and patients with IPF in INPULSIS



Kelly C et al. Effects of nintedanib in patients with progressive fibrosing RA-ILD in the INBUILD trial. EULAR, 2021



Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

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

Case report

A successful treatment of rheumatoid arthritis-related interstitial pneumonia with nintedanib

Tamaki Kakuwa*, Shinyu Izumi, Keita Sakamoto, Tomoyuki Suzuki, Motoyasu Iikura, Haruhito Sugiyama

Department of Respiratory Medicine, National Center for Global Health and Medicine, Japan

Efficacy in RA-UIP without joint involvement

Nintedanib for the treatment of refractory progressive rheumatoid arthritis–related interstitial lung disease: a real-life case series

Rheumatology key message

- Nintedanib can slow the decline of lung function in refractory progressive RA-ILD in clinical practice.

Seven RA-UIP patients, combined to LEF or MMF or TCZ and/or RTX

Hindawi
Case Reports in Medicine
Volume 2020, Article ID 6390749, 4 pages
https://doi.org/10.1155/2020/6390749

Case Report

Combination Therapy with Nintedanib and Sarilumab for the Management of Rheumatoid Arthritis Related Interstitial Lung Disease

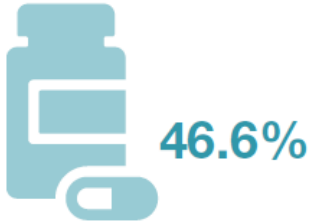
RA-UIP patient in combination with anti-IL-6

INBUILD: Patients taking DMARDs and/or glucocorticoids at baseline

Among patients taking DMARDs and/or glucocorticoids at baseline (n=131):

87.8%

were taking glucocorticoids



46.6%

were taking non-biologic DMARDS

15.3%

were taking biologic DMARDS

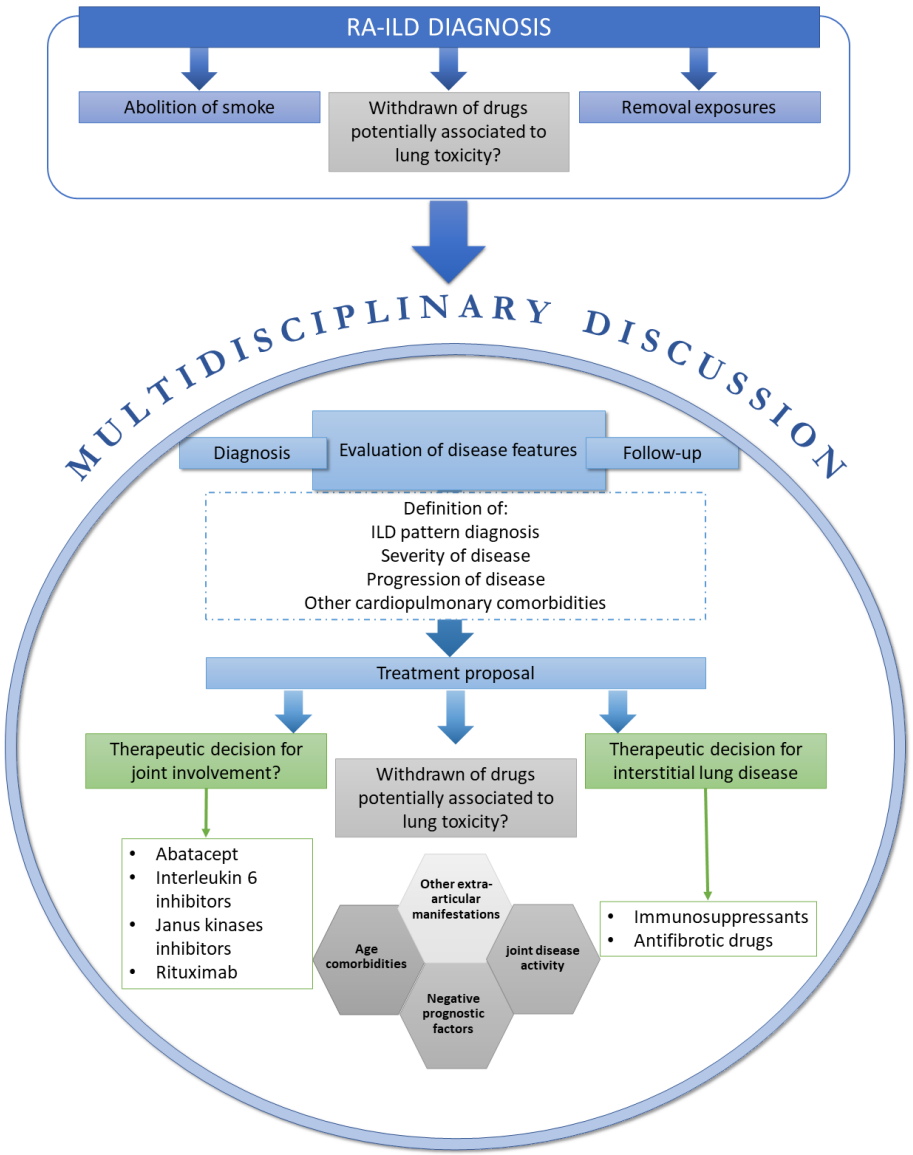
Most frequently used therapies:

Prednisone	37.4%
Prednisolone	35.1%
Methylprednisolone	8.4%
Meprednisone	3.1%

Hydroxychloroquine /sulphate	19.8%
Leflunomide	11.5%
Methotrexate	11.5%
Sulfasalazine	7.6%

Abatacept	4.6%
Etanercept	3.1%
Tocilizumab	3.1%

Therapies taken by ≥4 patients (3.1%) are shown. All but 1 patient taking glucocorticoids at baseline took <20 mg/day.
Aringer M et al. Efficacy and safety of nintedanib in patients with autoimmune disease-related interstitial lung diseases treated with DMARDs and/or glucocorticoids at baseline.



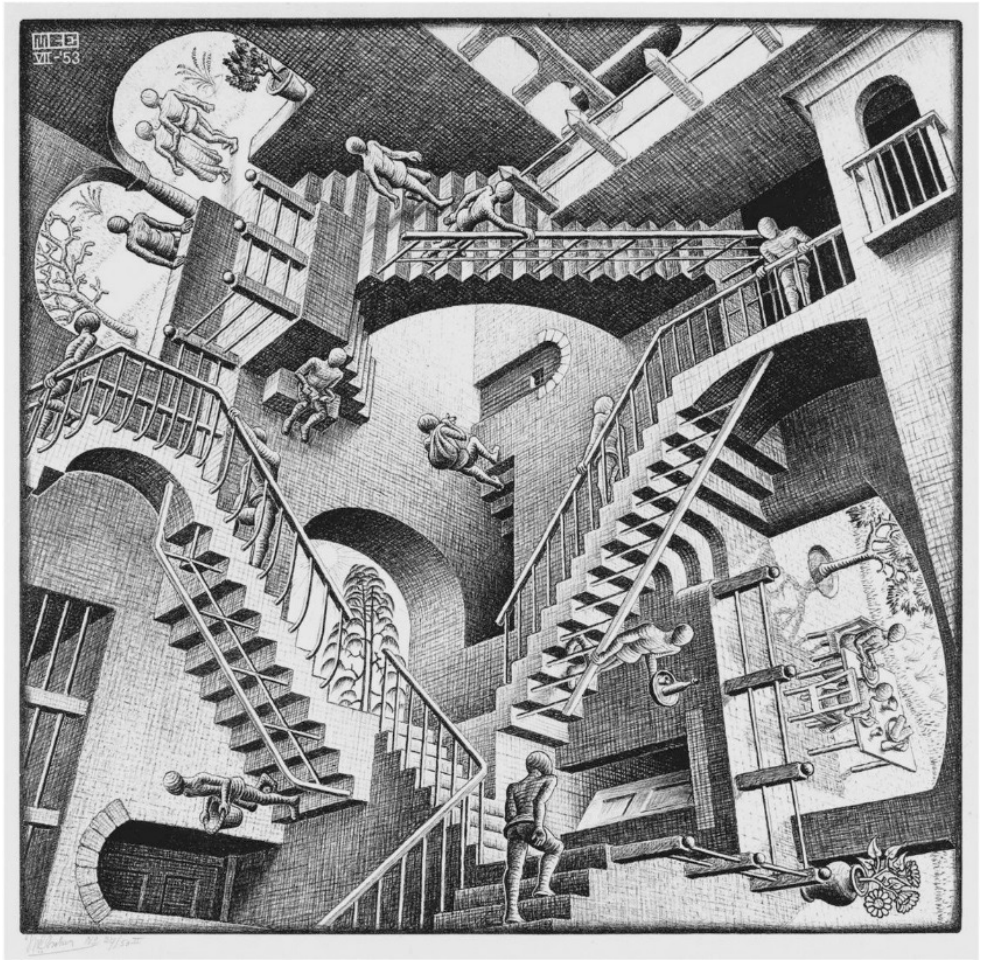
Lung involvement in rheumatoid arthritis is frequent and heterogeneous

Interstitial lung disease significantly impairs quality of life and survival of patients with rheumatoid arthritis

Chest HRCT is the milestone for the diagnosis of lung involvement

Multidisciplinary approach is needed for the treatment of rheumatoid arthritis related ILD

Manfredi A, et al. Expert Rev Clin Immunol. 2021;17:485-97



Ambulatorio multidisciplinare per le malattie rare del polmone

Pneumologia
dott. Stefania Cerri
dott. Dario Andrisani
dott. Filippo Gozzi

Reumatologia
dott. Andreina Manfredi
dott. Giulia Cassone
dott. Caterina Vacchi
prof. Marco Sebastiani

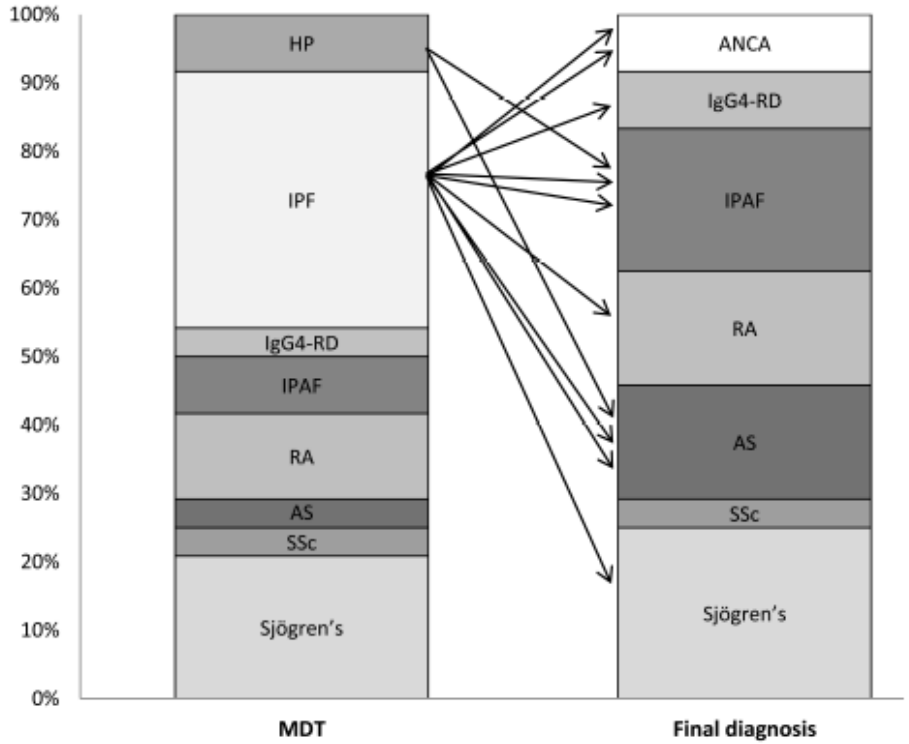
Cardiologia
dott. Francesca Coppi

Radiologia
dott. Giovanni Della Casa

Prima di venire qui, ero confuso su questo argomento. Dopo aver ascoltato la sua conferenza, io sono ancora confuso, ma a un livello più alto.

Enrico Fermi

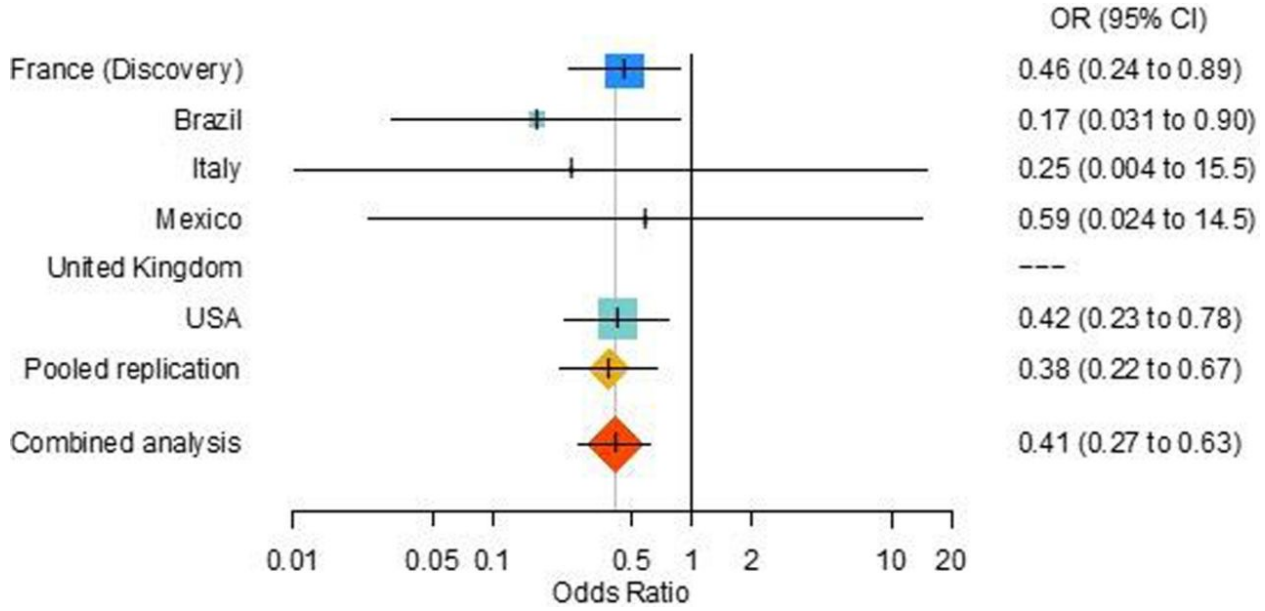
Changes in diagnosis for patients who were eventually diagnosed with a rheumatologically related condition



The rheumatological assessment reclassified 21% of the idiopathic pulmonary fibrosis as CTD. Moreover, the number of CTD-ILD with autoimmune features was increased by 77%

Levi Y et al. J. Rheumatol. 2018; 45: 1509-14

Methotrexate and rheumatoid arthritis associated interstitial lung disease



482 patients with RA-ILD and 741 patients with RA without ILD were included.
Combined estimate analysis revealed an **adjusted OR of 0.41** (95% CI, 0.27 – 0.63; P<.0001).

MTX ever users were less frequent among patients with RA-ILD compared to those without ILD, irrespective of chest high resolution computed tomography pattern.
In patients with RA-ILD, ILD onset was significantly delayed in MTX ever users compared to never users (11.5 ± 10.6 years and 3.7 ± 7.1 years, respectively; P<.0001).

Juge PA et al. *Ann Rheum Dis* 2020

Methotrexate and interstitial lung disease: controversies and questions. A narrative review of the literature

George E. Fragoulis [1,2,*], Richard Conway [3,4,*] and Elena Nikiphorou[5,6]

Overall there were 13 cases of MTX-pneumonitis reported in the 4544 MTX-treated patients across the included studies.
Cases of MTX-pneu were reported in 4 of the 22 studies. Intriguingly, however, **no RCTs of MTX in RA performed since 2001 had reported any cases of MTX-pneu**

A meta-analysis included 1640 patients, 818 receiving MTX and 812 comparators, with psoriasis, PsA and inflammatory bowel diseases.
No increase in overall respiratory adverse events with MTX use (RR 1.03, 95% CI 0.90, 1.17).

No increase in infectious adverse events (RR 1.02, 95% CI 0.88, 1.19)

No increase in non-infectious adverse events (RR 1.07, 95% CI 0.58, 1.96).