
# Το Nintedanib στη θεραπεία της διάμεσης πνευμονοπάθειας στα αυτοανοσα νοσήματα

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ΓΝΘ Ιπποκράτειο

## Δήλωση σύγκρουσης συμφερόντων

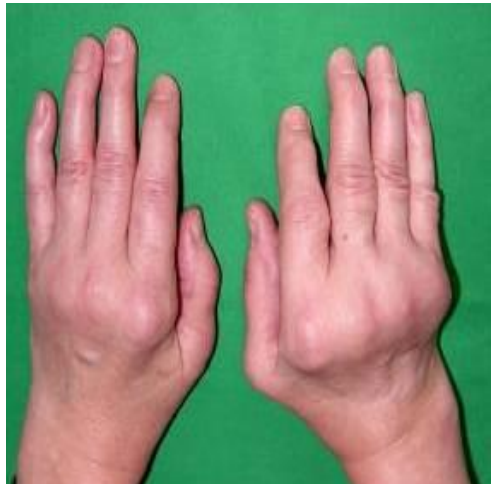
- Boehringer Ingelheim

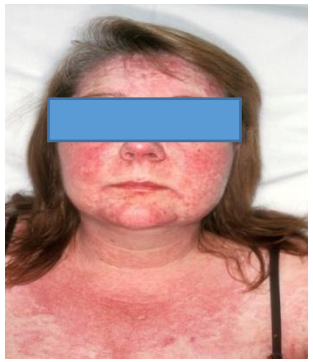
Εκπαιδευτικές-ερευνητικές-συμβουλευτικές επιχορηγήσεις την τελευταία διετία:

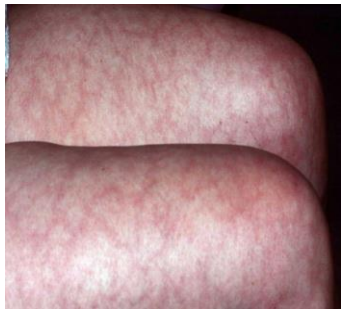
Abbvie, Amgen, Demo Hellas, Elpen, Genessis Pharma, JANSSEN, Gilead, ΚΟΠΕΡ, Lilly, Mylan, Novartis, UCB

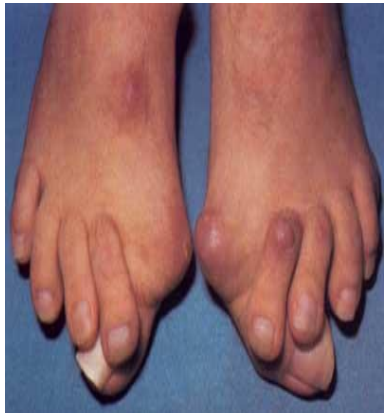
# CTD-ILDs

| CTD-ILD | Prevalence of CTD[1] | Prevalence of ILD[2] | Prevalence of ILD (UK) |
|---|---|---|---|
| SSc | 26* | 70–90% | ~35% |
| RA | 0.5–2%† | 4–68% | ~10% |
| SS | 3%‡ | 10–30% | ~2% |
| Mixed CTD | 3.8* | 20–85% | ~40% |
| PM/DM | Unknown | 15–70% | ~40% |
| SLE | 15–50* | 2–10% | ~2% |









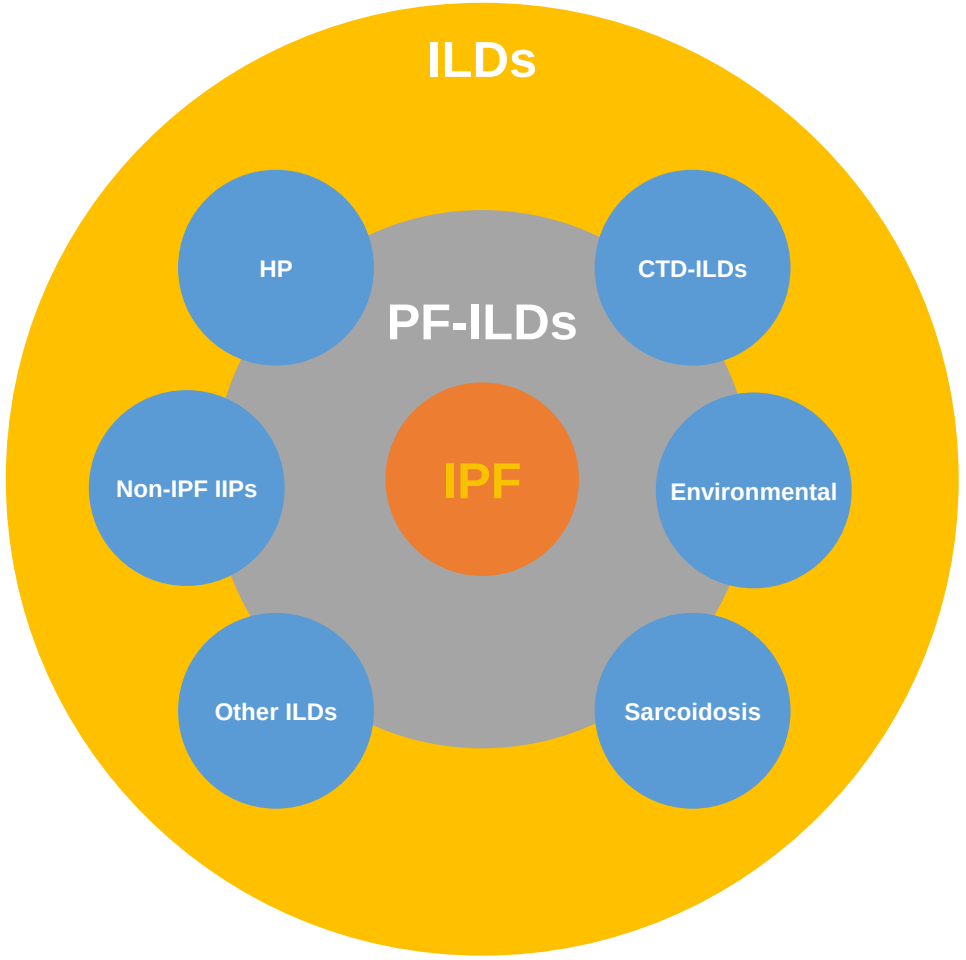
*Number of cases per 100,000 persons; †Percentage of the general population; ‡In patients aged >50 years

**1. Koo SM, Uh ST.** ***Korean J Intern Med*** **2017;32:600–10; 2. Wallace B** ***et al. Curr Opin Rheumatol*** **2016;28:236–45**

# Προοδευτικός φαινότυπος - Progressive fibrosing ILDs (PF-ILDs)

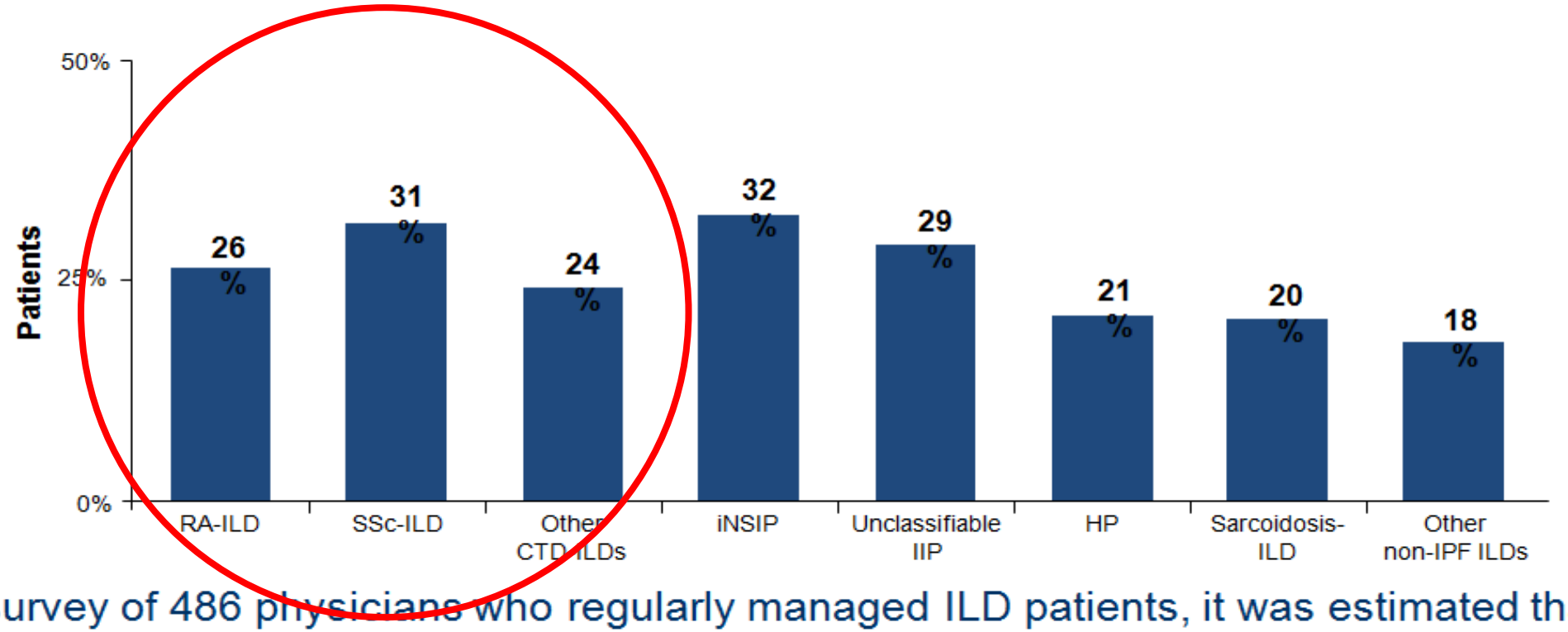
Patients with PF-ILDs show common disease behaviour irrespective of the clinical diagnosis:

- Progressive pulmonary fibrosis
- Declining lung function
- Worsening respiratory symptoms
- Worsening quality of life
- Early mortality




CTD: connective tissue disease, HP: hypersensitivity pneumonitis; IIP: idiopathic interstitial pneumonia; ILD: interstitial lung disease

# Up to one-third of patients with ILDs, including CTD-ILD, develop progressive fibrosing disease




From a survey of 486 physicians who regularly managed ILD patients, it was estimated that 18–32% of patients diagnosed with non-IPF ILD develop progressive fibrosis[1]

1. Wijsenbeek M *et al*. ATS 2018 International Conference. San Diego, USA, May 18–23, 2018; abstract A1678

# How Is Progression Defined in Progressive Fibrosing ILDs

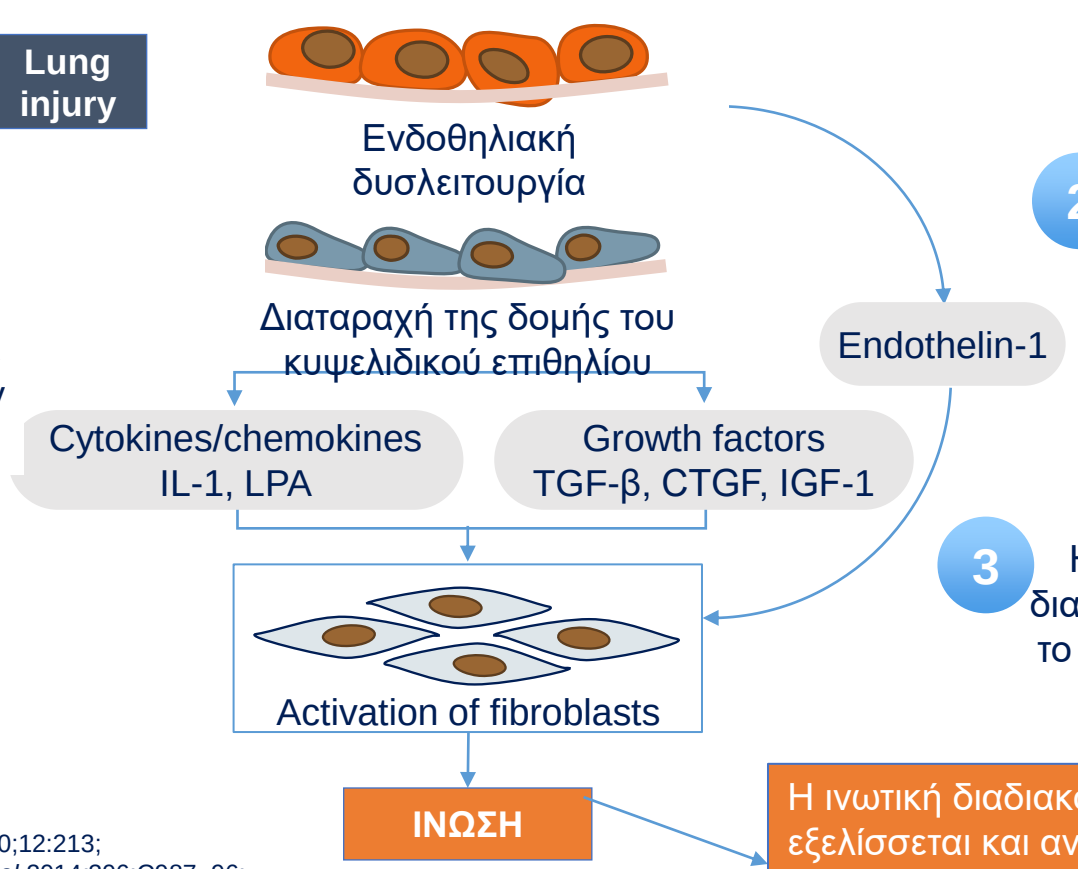
| Key criteria used in progressive fibrosing-ILD clinical trial for evidence of progression | |
|---|---|
| Worsening lung function | ≥10% relative decline in FVC % pred (clinically significant) |
| Or | ≥5 – <10% relative decline in FVC % pred (marginal decline) |
| Marginal decline in lung function AND worsening of respiratory symptoms | |
| Or marginal decline in lung function AND evidence of increasing fibrosis on chest HRCT imaging, despite treatment with unapproved meds used in clinical practice to treat ILD | |

Flaherty KR, et al. *BMJ Open Respir Res.* 2017;4:e000212.

# Fibrosing ILDs develop and progress via common pathobiological pathways

**1**

Βασικό εναρκτήριο γεγονός της πνευμονικής ίνωσης είναι η διαταραχή και επαναλαμβανόμενα τραύματα της πνευμονικής μικροκυκλοφορίας που οδηγούν σε βλάβη των ενδοθηλιακών κυττάρων και του κυψελιδικού επιθηλίου.




**2**

Η κυτταρική βλάβη οδηγεί σε έκκριση κυταροκινών, διαμεσολαβητών της φλεγμονής και αυξητικών παραγόντων και διαταραχές της αιμόστασης, με ενεργοποίηση του καταρράκτη της πήξης

**3**

Η ενεργοποίηση των ινοβλαστών και η διαφοροποίηση σε μυοϊνοβλάστες αποτελεί το βασικό γεγονός στην έναρξη και εξέλιξη της ίνωσης.[1]

Η ινωτική διαδιακσία αποτελεί μια δυναμική διαδικασία που εξελίσσεται και ανατροφοδοτείται και τελικά οδηγεί σα αύξηση και σε επέκταση της ινωτικής μάζας ανεξάρτητα του αρχικού γεγονότος που πυροδότησε την έναρξη της,[2–4]

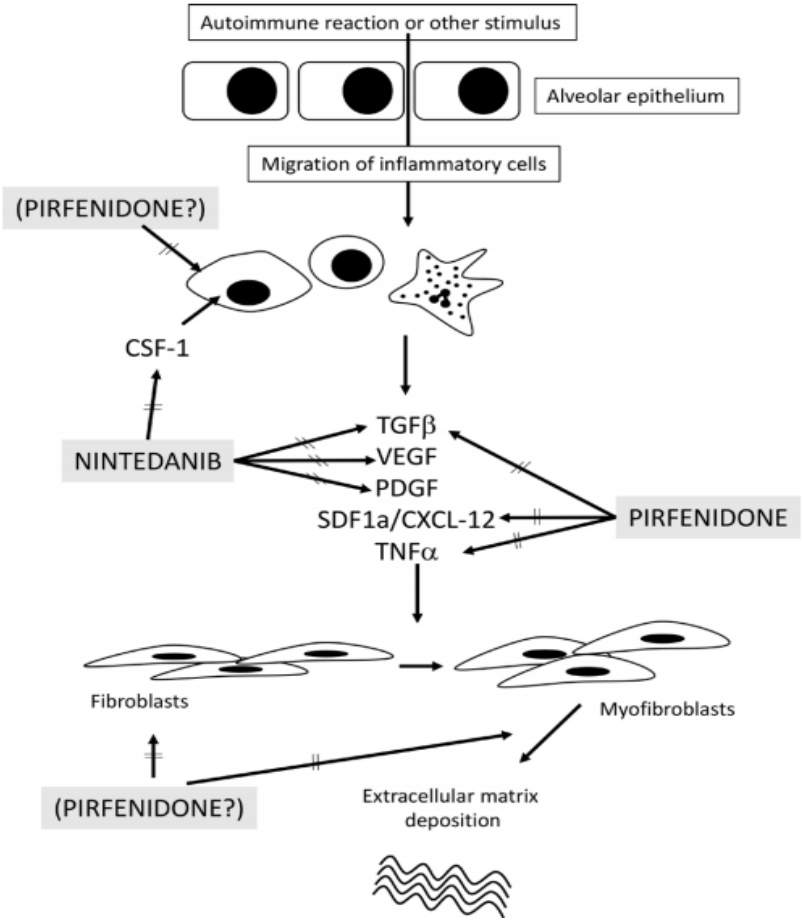

1. Castelino FV, Varga J. *Arthritis Res Ther* 2010;12:213;
2. Barkauskas CE *et al. Am J Physiol Cell Physiol* 2014;306:C987–96;
3. Liu F *et al. J. Cell Biol* 2010;190:693–706;
4. Parker MW *et al. J Clin Invest* 2014;124:1622–35

Annals of the Rheumatic Diseases

Review

# Mechanisms of progressive fibrosis in connective tissue disease (CTD)-associated interstitial lung diseases (ILDs)

Paolo Spagnolo ,[1] Oliver Distler ,[2] Christopher J Ryerson,[3] Argyris Tzouvelekis,[4] Joyce S Lee,[5] Francesco Bonella,[6] Demosthenes Bouros,[7] Anna-Maria Hoffmann-Vold ,[8] Bruno Crestani,[9,10] Eric L Matteson[11]




Lung alveoral epithelial injury and repeat repair

-Autoimmune dysregulation (CTD)

-Endothelial activation (SSc)

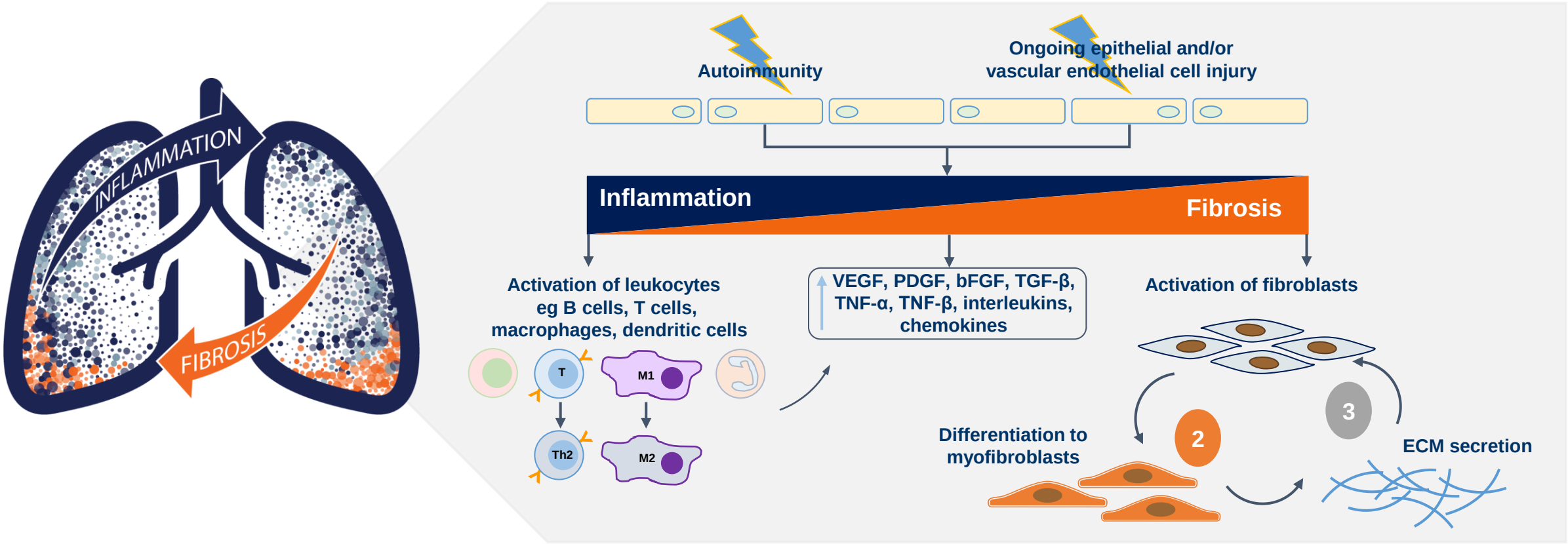
-Granuloma formation (sarcoidosis)

-Macrophage activation (asbestosis)

Genetic mechanisms driving progressive pulmonary fibrosis

Spagnolo P, et al. Ann Rheum Dis 2020;**0**:1–8. doi:10.1136/annrheumdis-2020-217230

# The pathogenesis of CTD-ILD involves the interplay of inflammation and fibrosis early in the disease course

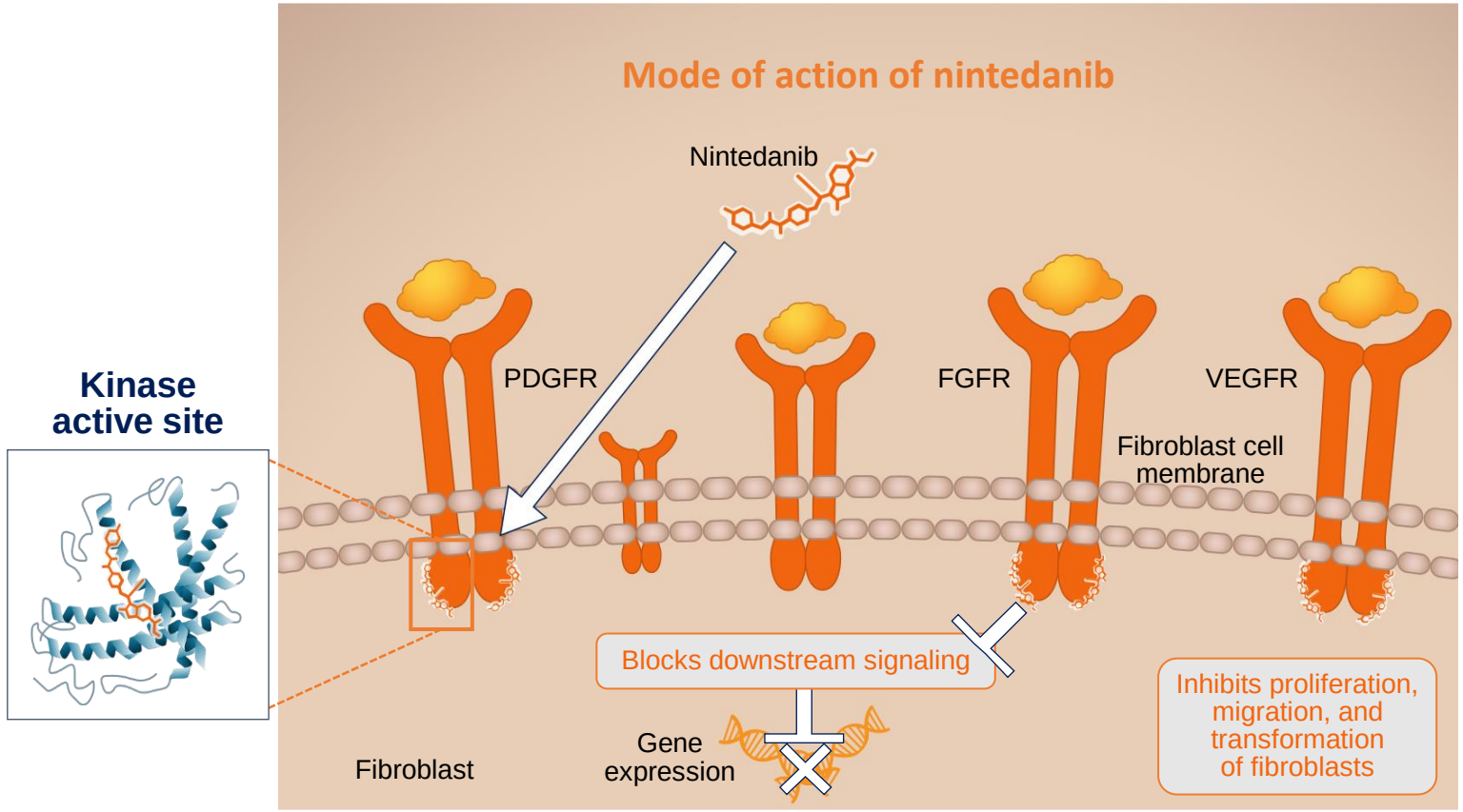



bFGF, basic fibroblast growth factor; CTD-ILD, connective tissue disease-associated interstitial lung disease; CTGF, connective tissue growth factor; M1, classically activated macrophage; M2, alternatively activated macrophage; PDGF, platelet-derived growth factor; TGF, transforming growth factor; Th2, type 2 T helper cell; TNF, tumor necrosis factor; VEGF, vascular endothelial growth factor

1. Bagnato G, Harari S. *Eur Respir Rev* 2015;24:102–14; 2. Castelino F, Varga J. *Arthritis Res Ther* 2010;12:213; 3. Dellaripa PF. *Clin Immunol* 2018;186:71–3; 4. Wells A, Denton C. 2014 *Nat Rev Rheumatol* 2014;10:728–39

# Nintedanib, a tyrosine kinase inhibitor with anti-inflammatory and anti-fibrotic activity, slows the progression of fibrosing ILD

- Oral small-molecule tyrosine kinase inhibitor (TKI)
- Inhibits downstream signaling pathways crucial for the proliferation, migration, transformation of fibroblasts, and collagen production
- It exerts pleiotropic effects, including anti-fibrotic, anti-inflammatory, and anti-angiogenic activity




Nintedanib Summary of Product Characteristics.

Annals of the Rheumatic Diseases

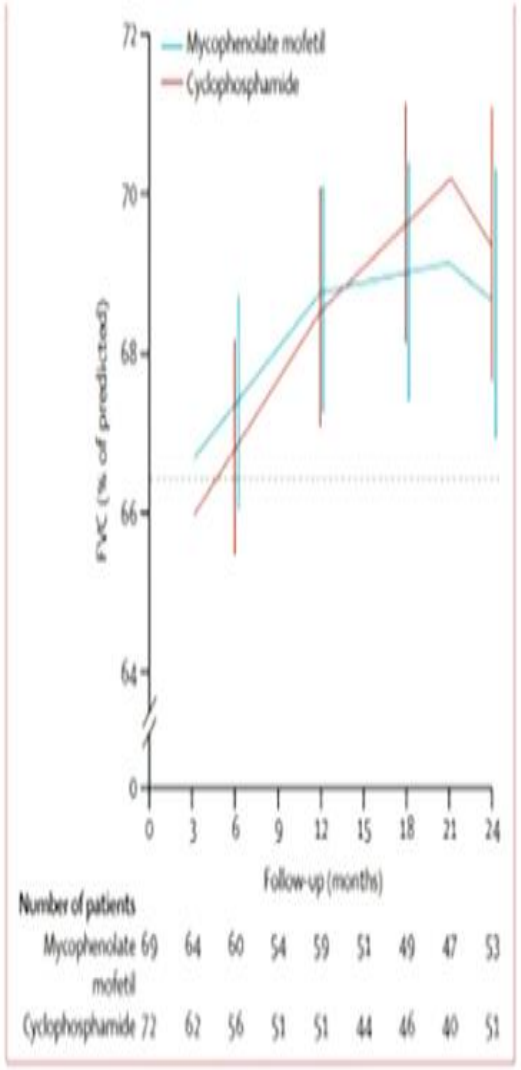
# Update of EULAR recommendations for the treatment of systemic sclerosis

Otylia Kowal-Bielecka,[1] Jaap Fransen,[2] Jerome Avouac,[3] Mike Becker,[4,5] Agnieszka Kulak,[1] Yannick Allanore,[3] Oliver Distler,[5] Philip Clements,[6] Maurizio Cutolo,[7] Laszlo Czirjak,[8] Nemanja Damjanov,[9] Francesco del Galdo,[10] Christopher P Denton,[11] Jörg H W Distler,[12] Ivan Foeldvari,[13] Kim Figelstone,[14] Marc Frerix,[15] Daniel E Furst,[6] Serena Guiducci,[16] Nicolas Hunzelmann,[17] Dinesh Khanna,[18] Marco Matucci-Cerinic,[16] Ariane L Herrick,[19,20] Frank van den Hoogen,[2] Jacob M van Laar,[21] Gabriela Riemekasten,[22] Richard Silver,[23] Vanessa Smith,[24] Alberto Sulli,[7] Ingo Tarner,[15] Alan Tyndall,[25] Joep Welling,[26] Frederic Wigley,[27] Gabriele Valentini,[28] Ulrich A Walker,[25] Francesco Zulian,[29] Ulf Müller-Ladner,[15] EUSTAR Coauthors

2017;**76**:1327–1339.

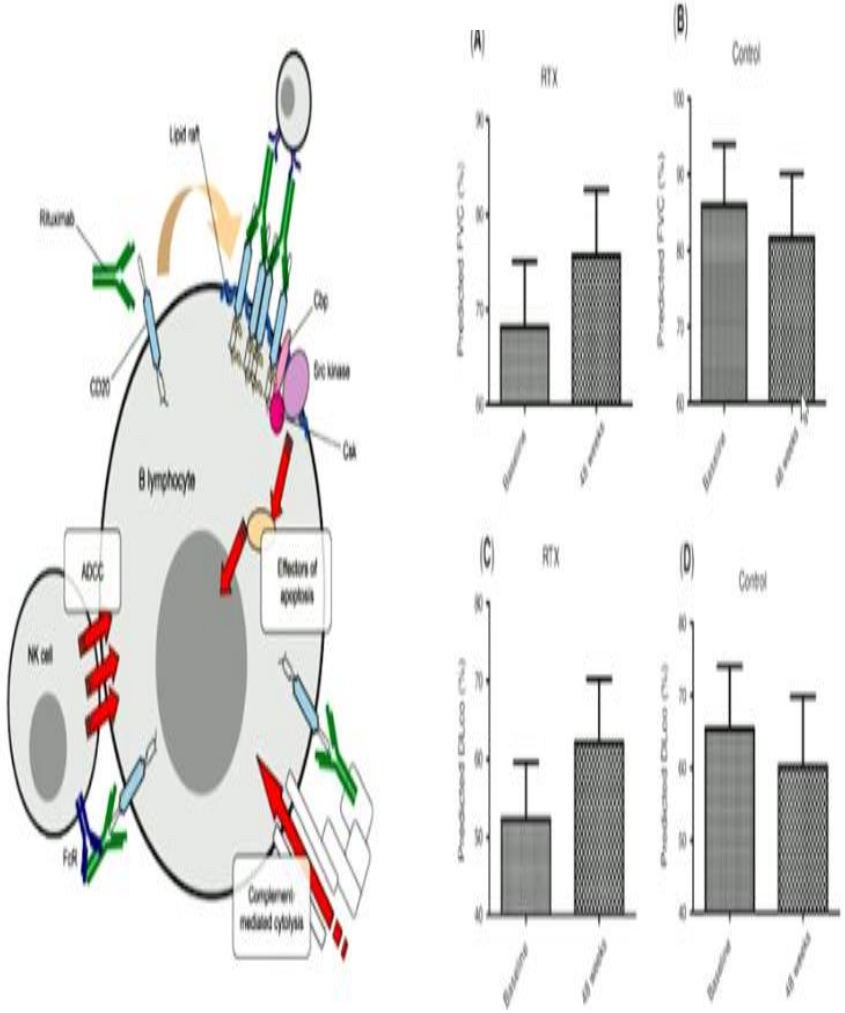
| Organ involvement | Recommendation | Strength of recommendation |
|---|---|---|
| IV. Skin and lung disease | In view of the results from two high-quality RCTs and despite its known toxicity, cyclophosphamide should be considered for treatment of SSc-ILD, in particular for patients with SSc with progressive ILD. | A |
| | Regarding HSCT, two RCTs have shown improvement of skin involvement and stabilisation of lung function in patients with SSc and one large RCT reports improvement in event-free survival in patients with SSc as compared with cyclophosphamide in both trials. HSCT should be considered for treatment of selected patients with rapidly progressive SSc at risk of organ failure. In view of the high risk of treatment-related side effects and of early treatment-related mortality, careful selection of patients with SSc for this kind of treatment and the experience of the medical team are of key importance. | A |

## MYCOPHENOLATE MOPHETYL



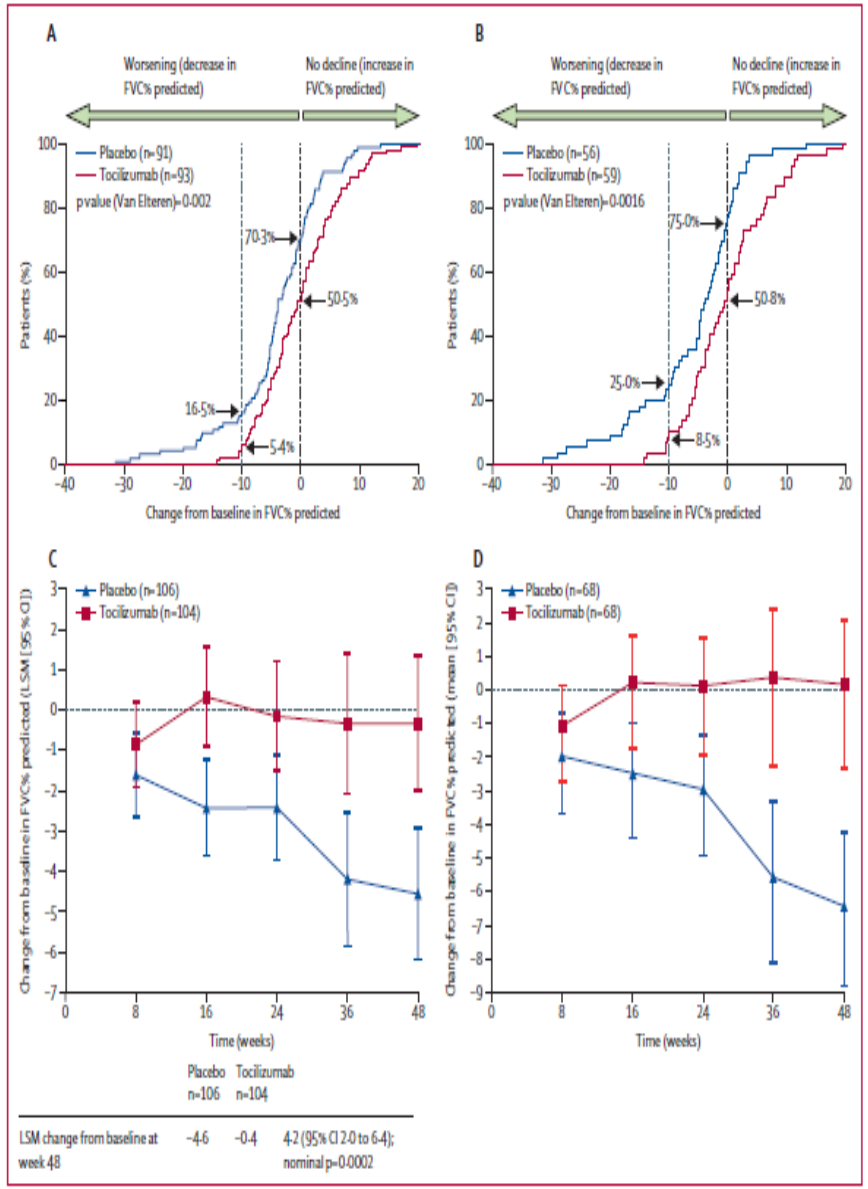

Taskhin D et al Lancet Respir Med 2016

## RITUXIMAB



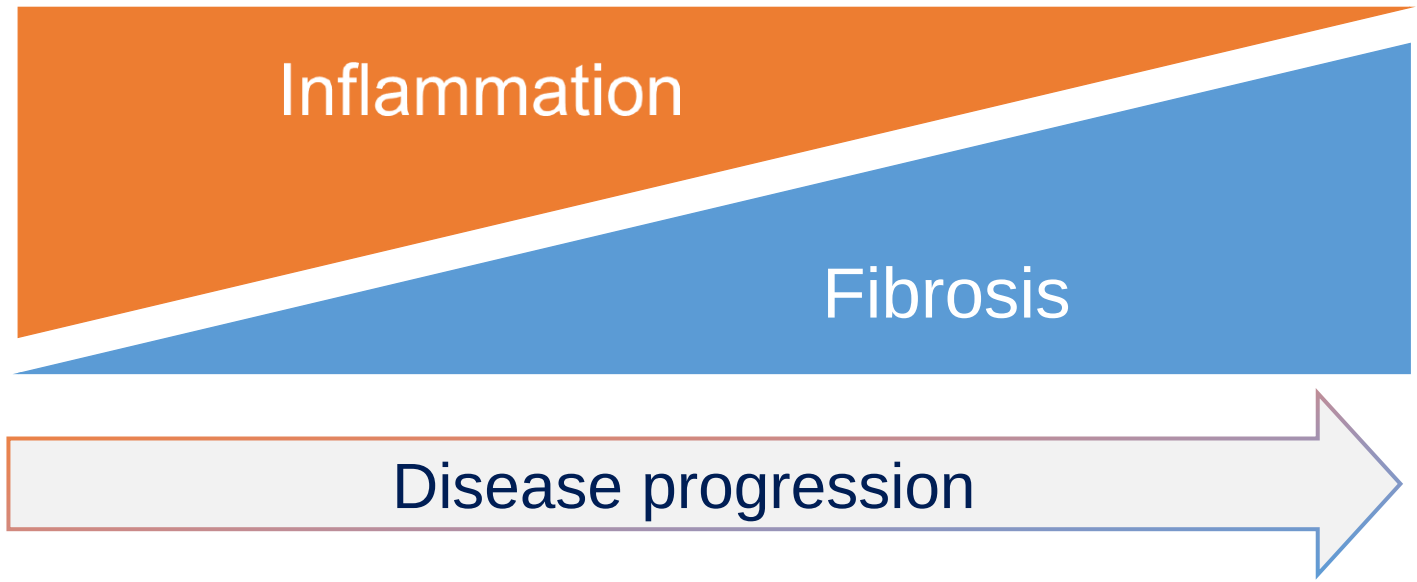

Daoussis D et al, Rheumatology 2009

## TOCILIZUMAB




Khanna D et al, Lancet Respir Med 2021

# The pathogenesis of CTD-ILD involves the interplay of inflammation and fibrosis early in the disease course




Currently, the standard of care is immunosuppresive therapy; there is an unmet need for a pharmacological treatment that targets mechanisms beyond inflammation[2,3]


- 1. Saketkoo LA *et al. J Scleroderm Relat Dis* 2020;5:48–60; 2. Wells AU. *Presse Med* 2014;43:e329–43; 3. Distler O *et al. Exp Rev Clin Immunol* 2019;15:1009–17; 4. Das A *et al. Exp Rev Respir Med* 2019;13:357–67

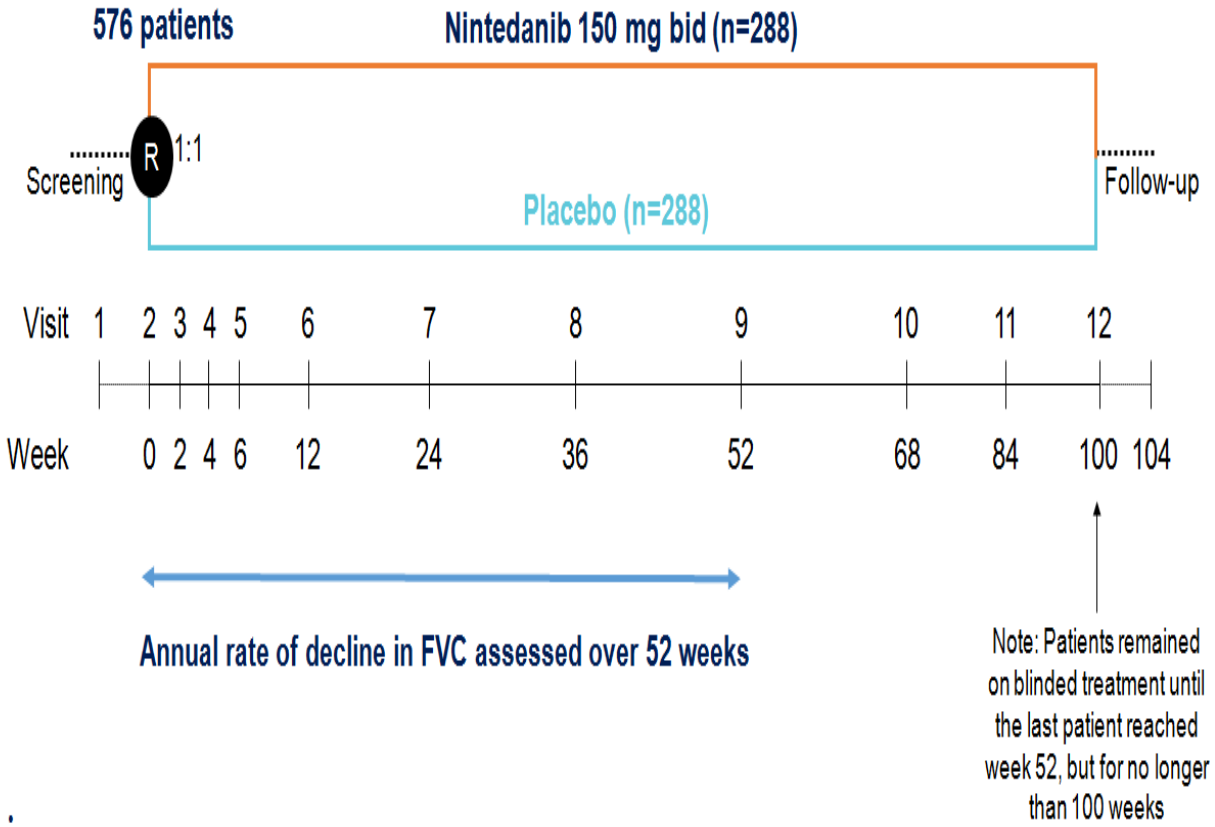
The NEW ENGLAND JOURNAL of MEDICINE

# Nintedanib for Systemic Sclerosis–Associated Interstitial Lung Disease

2019;27;380(26):2518-28

Oliver Distler, M.D., Kristin B. Highland, M.D., Martina Gahlemann, M.D., Arata Azuma, M.D., Aryeh Fischer, M.D., Maureen D. Mayes, M.D., Ganesh Raghu, M.D., Wiebke Sauter, Ph.D., Mannaig Girard, M.Sc., Margarida Alves, M.D., Emmanuelle Clerisme-Beaty, M.D., Susanne Stowasser, M.D., Kay Tetzlaff, M.D., Masataka Kuwana, M.D., and Toby M. Maher, M.D., for the SENSCIS Trial Investigators*

## SENSCIS was a Phase III, double-blinded, randomized, placebo-controlled trial




✓Patients with SSc with first non-Raynaud symptom <7 years before screening

✓Extent of fibrotic ILD ≥10% on a high-resolution computed tomography (HRCT) scan

✓FVC ≥40% predicted

✓DLco 30–89% predicted

✓Patients on prednisone ≤10 mg/day and/or stable therapy with mycophenolate or methotrexate for ≥6 months prior to randomization were allowed to participate

**No longitudinal assessment of progression was required for inclusion in the trial**

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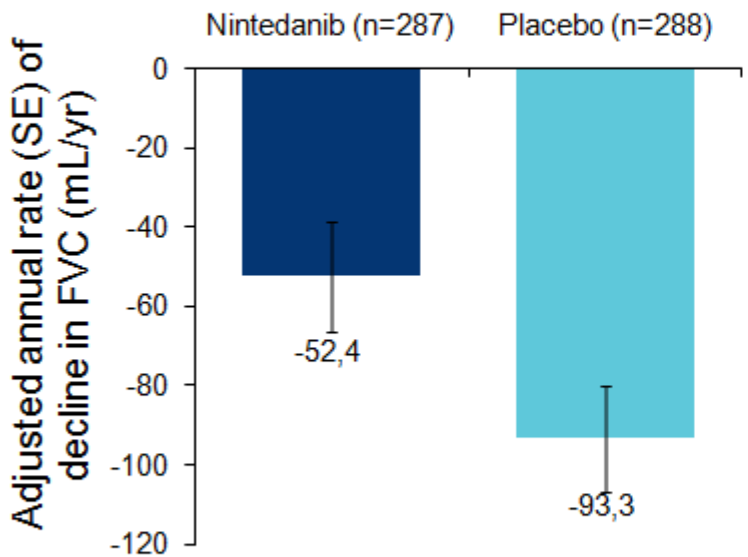
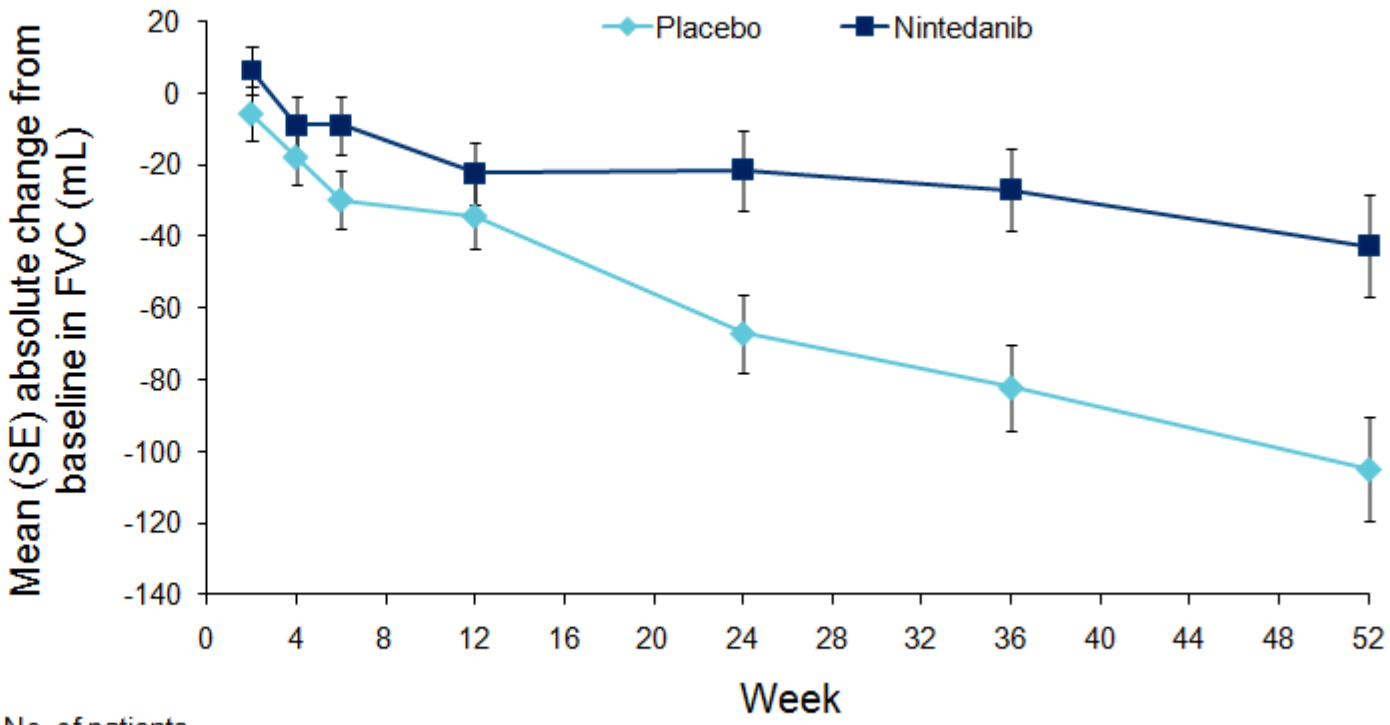
## Annual rate of decline in FVC (mL/yr) (primary endpoint)




Difference: 41.0 mL/yr
(95% CI: 2.9, 79.0); *P*=0.04
**Relative reduction: 44%**

## Change from baseline in FVC (mL) over 52 weeks*




No. of patients

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Nintedanib | 288 | 283 | 281 | 273 | | 278 | | 265 | | 262 | | | 241 |
| Placebo | 288 | 283 | 281 | 280 | | 283 | | 280 | | 268 | | | 257 |

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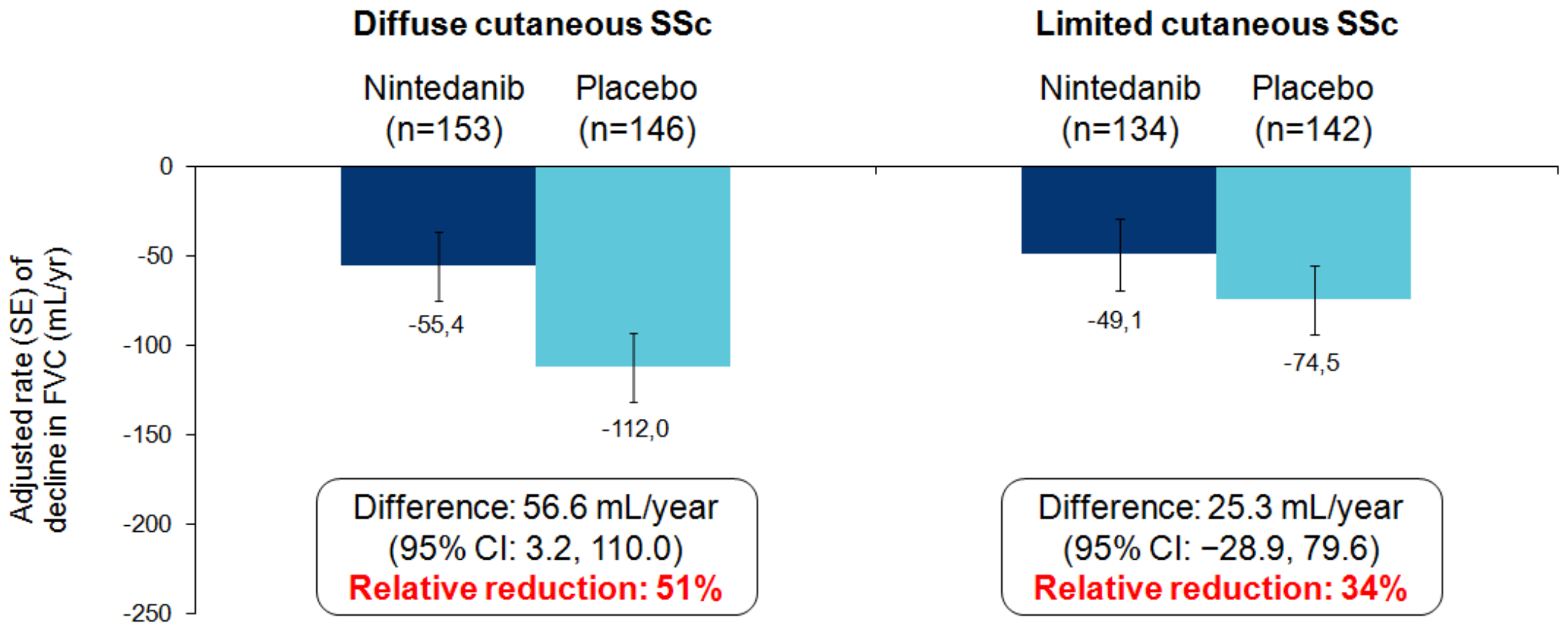

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2019 Jun 27;380(26):2518-28

- ✓FVC ≥40% predicted
- ✓DLco 30–89% predicted

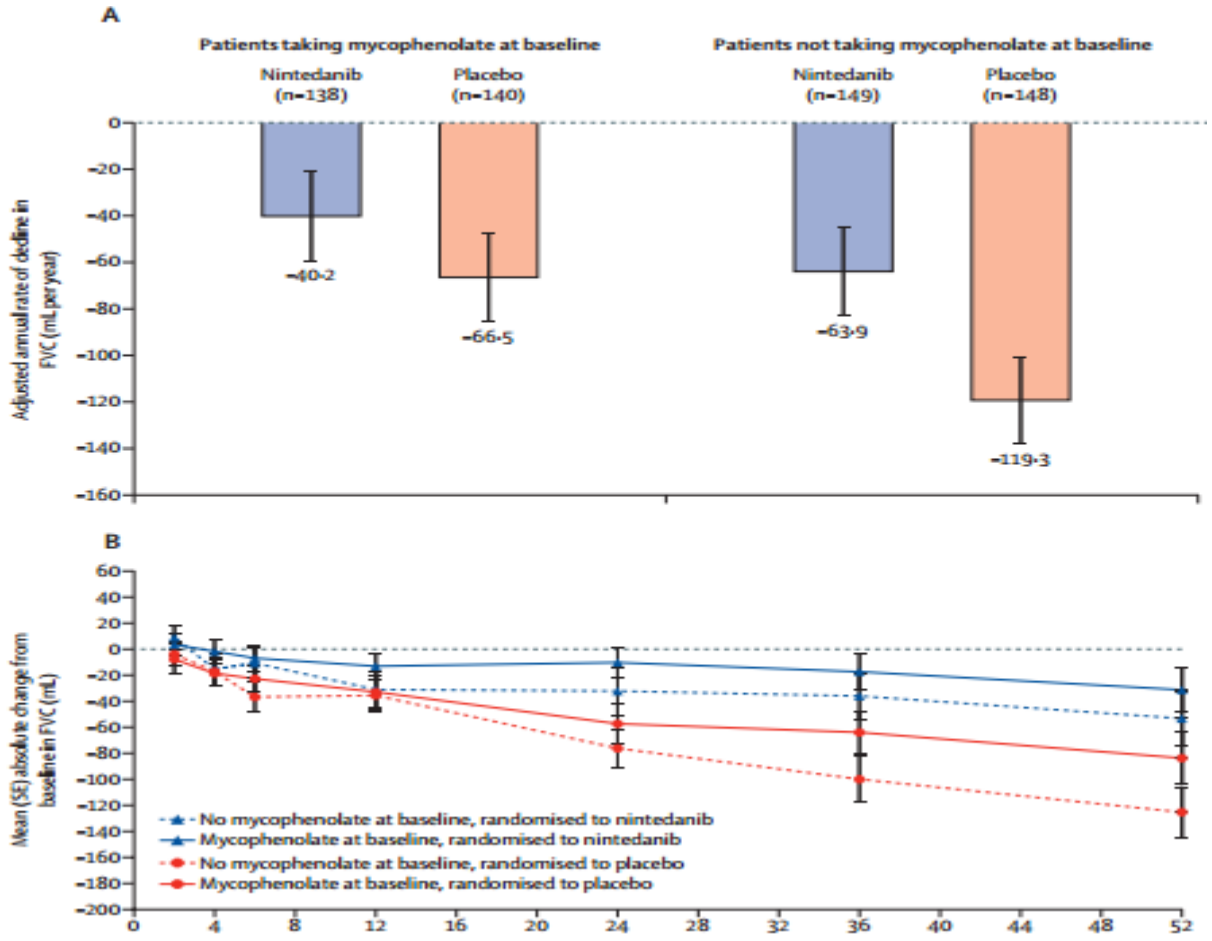
**Table 1. Baseline Characteristics of the Patients.***

| Characteristic | Nintedanib (N=288) | Placebo (N=288) |
|---|---|---|
| Female sex — no. (%) | 221 (76.7) | 212 (73.6) |
| Age — yr | 54.6±11.8 | 53.4±12.6 |
| Diffuse cutaneous systemic sclerosis — no. (%) | 153 (53.1) | 146 (50.7) |
| Years since the onset of the first non-Raynaud's symptom | | |
| Median | 3.4 | 3.5 |
| Range | 0.3 to 7.1 | 0.4 to 7.2 |
| Extent of fibrosis of the lungs on high-resolution CT — % | 36.8±21.8 | 35.2±20.7 |
| FVC — ml | 2459±736 | 2541±816 |
| FVC — % of predicted value | 72.4±16.8 | 72.7±16.6 |
| $DL_{CO}$ — % of predicted value† | 52.9±15.1 | 53.2±15.1 |
| Antitopoisomerase antibody positive — no. (%)‡ | 173 (60.1) | 177 (61.5) |
| Modified Rodnan skin score§ | 11.3±9.2 | 10.9±8.8 |
| Patients with diffuse cutaneous systemic sclerosis | 17.0±8.7 | 16.3±8.9 |
| Patients with limited cutaneous systemic sclerosis | 4.9±4.2 | 5.4±4.1 |
| Total score on the SGRQ¶ | 40.7±20.2 | 39.4±20.9 |
| Score on the HAQ-DI‖ | 0.65±0.70 | 0.55±0.58 |
| Scaled score on the FACIT-Dyspnea questionnaire** | 47.01±9.64 | 45.67±9.90 |
| Receiving mycophenolate — no. (%) | 139 (48.3) | 140 (48.6) |
| Receiving methotrexate — no. (%) | 23 (8.0) | 15 (5.2) |

THE LANCET
Respiratory Medicine
2021;9: 96–106

# Efficacy and safety of nintedanib in patients with systemic sclerosis-associated interstitial lung disease treated with mycophenolate: a subgroup analysis of the SENSCIS trial

*Kristin B Highland*, Oliver Distler*, Masataka Kuwana, Yannick Allanore, Shervin Assassi, Arata Azuma, Arnaud Bourdin, Christopher P Denton, Jörg H W Distler, Anna Maria Hoffmann-Vold, Dinesh Khanna, Maureen D Mayes, Ganesh Raghu, Madelon C Vonk, Martina Gahlemann, Emmanuelle Clerisme-Beaty, Mannaig Girard, Susanne Stowasser, Donald Zoz, Toby M Maher, on behalf of the SENSCIS trial investigators†*




| | Patients taking mycophenolate at baseline | | Patients not taking mycophenolate at baseline | |
|---|---|---|---|---|
| | Nintedanib (n=139) | Placebo (n=140) | Nintedanib (n=149) | Placebo (n=148) |
| Any adverse event* | 136 (98%) | 135 (96%) | 147 (99%) | 141 (95%) |
| Most frequent adverse events† | | | | |
| Diarrhoea | 106 (76%) | 48 (34%) | 112 (75%) | 43 (29%) |
| Nausea | 43 (31%) | 23 (16%) | 48 (32%) | 16 (11%) |
| Skin ulcer | 22 (16%) | 23 (16%) | 31 (21%) | 27 (18%) |
| Vomiting | 32 (23%) | 17 (12%) | 39 (26%) | 13 (9%) |
| Cough | 20 (14%) | 33 (24%) | 14 (9%) | 19 (13%) |
| Nasopharyngitis | 10 (7%) | 22 (16%) | 26 (17%) | 27 (18%) |
| Upper respiratory tract infection | 19 (14%) | 25 (18%) | 14 (9%) | 10 (7%) |
| Abdominal pain | 14 (10%) | 6 (4%) | 19 (13%) | 15 (10%) |
| Fatigue | 19 (14%) | 14 (10%) | 12 (8%) | 6 (4%) |
| Headache | 16 (12%) | 15 (11%) | 11 (7%) | 9 (6%) |
| Urinary tract infection | 16 (12%) | 11 (8%) | 8 (5%) | 12 (8%) |
| Weight decreased | 10 (7%) | 4 (3%) | 24 (16%) | 8 (5%) |
| Decreased appetite | 14 (10%) | 10 (7%) | 13 (9%) | 2 (1%) |
| Severe adverse event | 28 (20%) | 18 (13%) | 24 (16%) | 18 (12%) |
| Serious adverse event | 36 (26%) | 22 (16%) | 33 (22%) | 40 (27%) |
| Fatal adverse event | 3 (2%) | 2 (1%) | 2 (1%) | 2 (1%) |
| Adverse event leading to treatment discontinuation | 15 (11%) | 9 (6%) | 31 (21%) | 16 (11%) |

Data are n (%) of patients with at least one such adverse event. *Adverse events reported over 52 weeks (or until 28 days after last study drug intake for patients who discontinued study drug before week 52). †Adverse events that were reported in >10% of participants in any of these subgroups are shown.

*Table 3:* Adverse events in subgroups by use of mycophenolate at baseline

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## Excluded

Patients with severe PAH

-Cardiac index < 2lt/min/$m^2$

- Parental therapy with epoprostenol/tepronistil

Patients with active hemorrhage or history GI bleeding

In patients with full-dose therapeutic anticoagulation estimation of the balance between risks and anticipated benefits is required

Annals of the Rheumatic Diseases

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CLINICAL SCIENCE

# Safety and tolerability of nintedanib in patients with systemic sclerosis-associated interstitial lung disease: data from the SENSCIS trial

James R Seibold ,[1] Toby M Maher,[2,3,4] Kristin B Highland,[5] Shervin Assassi ,[6] Arata Azuma,[7] Laura Kathleen Hummers,[8] Ulrich Costabel,[9] Ute von Wangenheim,[10] Veronika Kohlbrenner,[11] Martina Gahlemann,[12] Margarida Alves,[13] Oliver Distler ,[14] on behalf of the SENSCIS trial investigators

2020 Nov;79(11):1478-1484.

**Table 2** Adverse events leading to permanent treatment discontinuation in the SENSCIS trial

| | Nintedanib (n=288) | Placebo (n=288) |
|---|---|---|
| Any adverse event(s) leading to permanent treatment discontinuation | 46 (16.0) | 25 (8.7) |
| Most frequent adverse event(s) leading to permanent treatment discontinuation* | | |
| Diarrhoea | 20 (6.9) | 1 (0.3) |
| Nausea | 6 (2.1) | 0 |
| Vomiting | 4 (1.4) | 1 (0.3) |
| Abdominal pain upper | 3 (1.0) | 1 (0.3) |
| Alanine aminotransferase increased | 2 (0.7) | 0 |
| Progression of ILD† | 3 (1.0) | 3 (1.0) |

| Treatment | (%) |
|---|---|
| Gastric acid related disorders | 79.5 |
| Antihypertensives | 64,1 |
| Pain killers | 53,9 |
| Steroids | 49,8 |
| Antiplatelet therapy | 30,1 |
| MMF | 48,8 |
| Methotrexate | 6 |

| Patients with PAH | | |
|---|---|---|
| | Nintedanib (n=23) | Placebo (n=29) |
| Worsening PAH | 1 | 1 |
| Cardiac failure | 0 | 0 |
| Pulmonary hemorrhage | 0 | 0 |

In the nintedanib and placebo groups respectively, serious adverse events occurred in higher proportions of patients with PH (34.8% and 34.5%) than without PH (23.0% vs 20.1%)

# Overview of the Management of SSc-ILD

## Non-pharmacologic & adjunct therapy

- Smoking cessation
- Supplemental oxygen
- Pulmonary rehabilitation
- GERD management
- Severe dyspnea symptom control

## Pharmacologic

### Immunomodulatory

- MMF
- CYC
- AZA
- Tocilizumab
- Rituximab
- Low dose steroids

### Antifibrotic

- Nintedanib

## Selected populations

- Autologous hematopoietic stem cell transplantation
- Lung transplantation

JSRD | Journal of Scleroderma and Related Disorders

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SAGE

# Treatment of systemic sclerosis–associated interstitial lung disease: Lessons from clinical trials

David Roofeh[1], Oliver Distler[2], Yannick Allanore[3], Christopher P Denton[4] and Dinesh Khanna[1,5]

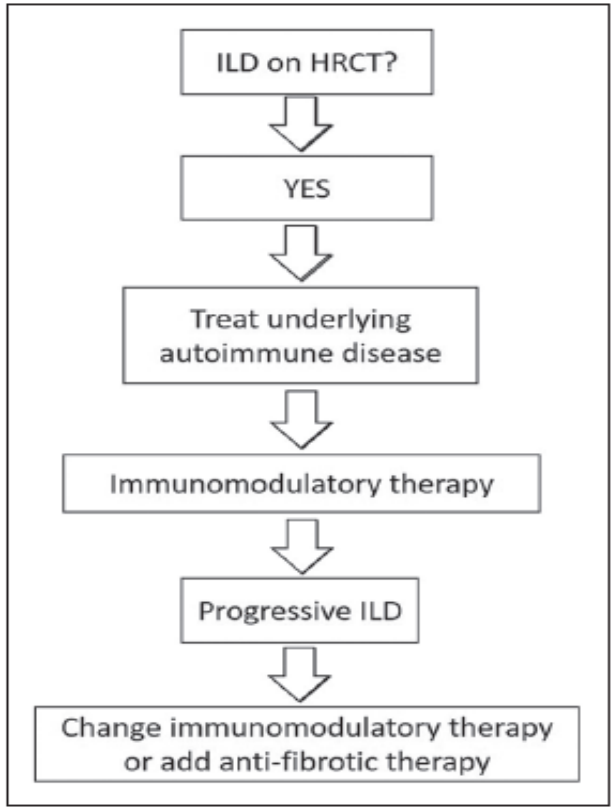



**Figure 1.** Treatment strategy 1: general management of early SSc, including ILD.

The NEW ENGLAND JOURNAL of MEDICINE

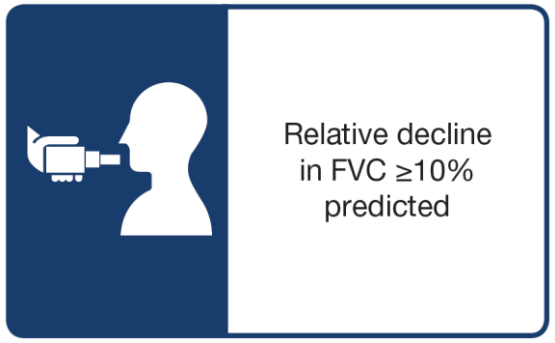
ORIGINAL ARTICLE

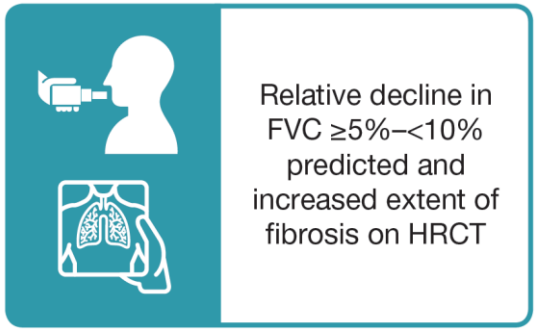
# Nintedanib in Progressive Fibrosing Interstitial Lung Diseases

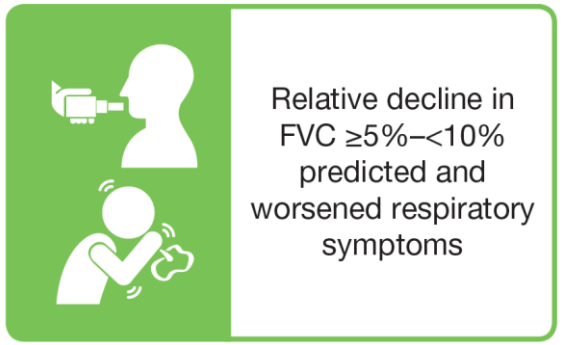
K.R. Flaherty, A.U. Wells, V. Cottin, A. Devaraj, S.L.F. Walsh, Y. Inoue, L. Richeldi, M. Kolb, K. Tetzlaff, S. Stowasser, C. Coeck, E. Clerisme-Beaty, B. Rosenstock, M. Quaresma, T. Haeufel, R.-G. Goeldner, R. Schlenker-Herceg, and K.K. Brown, for the INBUILD Trial Investigators*

N Engl J Med 2019;381:1718-27

- Physician-diagnosed ILD other than IPF, reticular abnormality with traction bronchiectasis (with or without honeycombing) of >10% extent on HRCT, FVC ≥45% predicted, DLco ≥30%–<80% predicted
- Met ≥1 of the following criteria for ILD progression in the 24 months before screening, despite management deemed appropriate in clinical practice:

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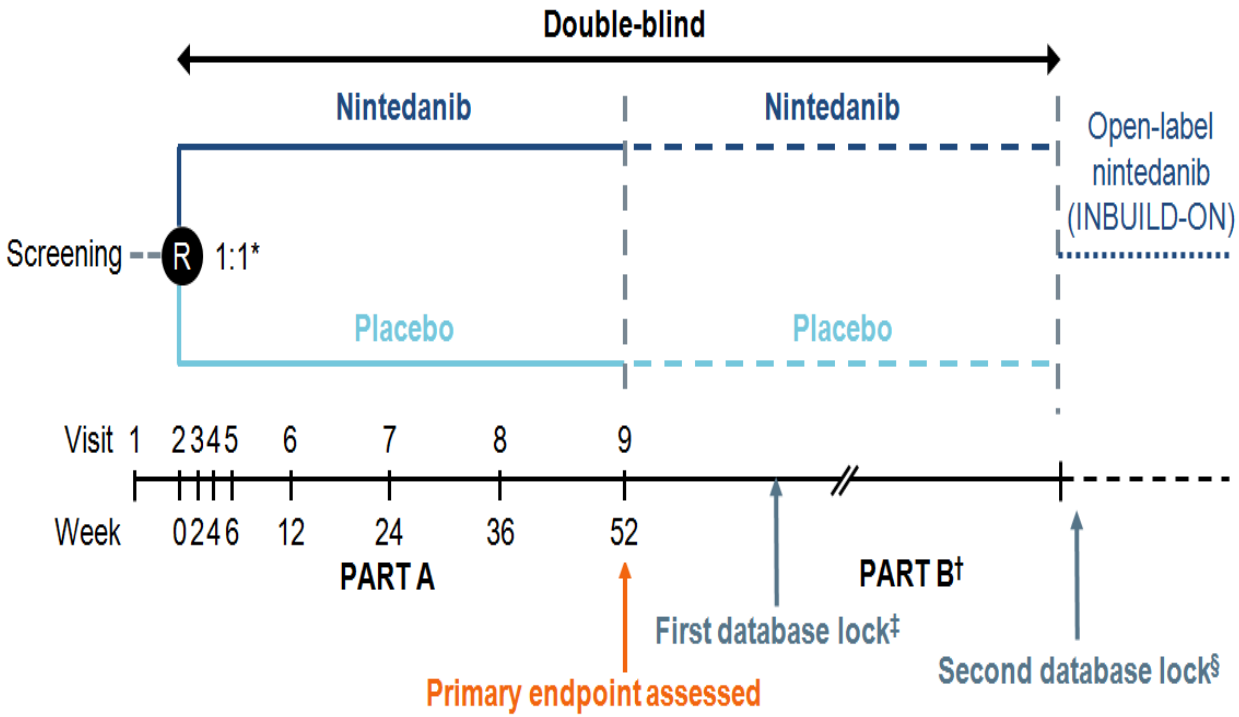
N Engl J Med 2019;381:1718-27

## INBUILD trial design



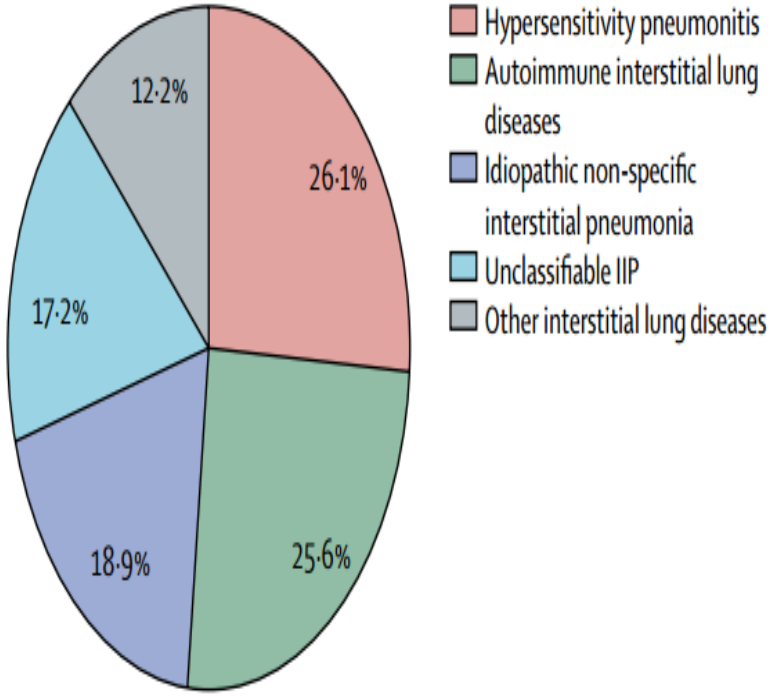

✓Patients taking azathioprine; cyclosporine; mycophenolate mofetil, tacrolimus oral glucocorticoids >20 mg/day; the combination of oral glucocorticoids,azathioprine and N-acetylcysteine; cyclophosphamide; or rituximab were not eligible

✓Initiation of these restricted therapies was allowed after 6 months of trial treatment in patients with deterioration of ILD or connective tissue disease

✓Apart from these restricted therapies, there was no limit on the use of stable doses of biologic or non-biologic DMARDs

# INBUILD: Clinical ILD diagnoses in overall population

| | Nintedanib (n=332) | Placebo (n=331) |
|---|---|---|
| Hypersensitivity pneumonitis | 84 (25.3) | 89 (26.9) |
| Autoimmune ILDs | 82 (24.7) | 88 (26.6) |
| Rheumatoid arthritis-associated ILD | 42 (12.7) | 47 (14.2) |
| Systemic sclerosis-associated ILD | 23 (6.9) | 16 (4.8) |
| Mixed connective tissue disease-associated ILD | 7 (2.1) | 12 (3.6) |
| Other autoimmune ILDs | 10 (3.0) | 13 (3.9) |
| Idiopathic non-specific interstitial pneumonia | 64 (19.3) | 61 (18.4) |
| Unclassifiable IIP | 64 (19.3) | 50 (15.1) |
| Other fibrosing ILDs* | 38 (11.4) | 43 (13.0) |




Data are n (%) of patients. *In the nintedanib and placebo groups, respectively, 21 (6.3%) and 18 (5.4%) patients had exposure-related ILDs and 4 (1.2%) and 8 (2.4%) patients had sarcoidosis. IIP, idiopathic interstitial pneumonia.

The NEW ENGLAND JOURNAL of MEDICINE

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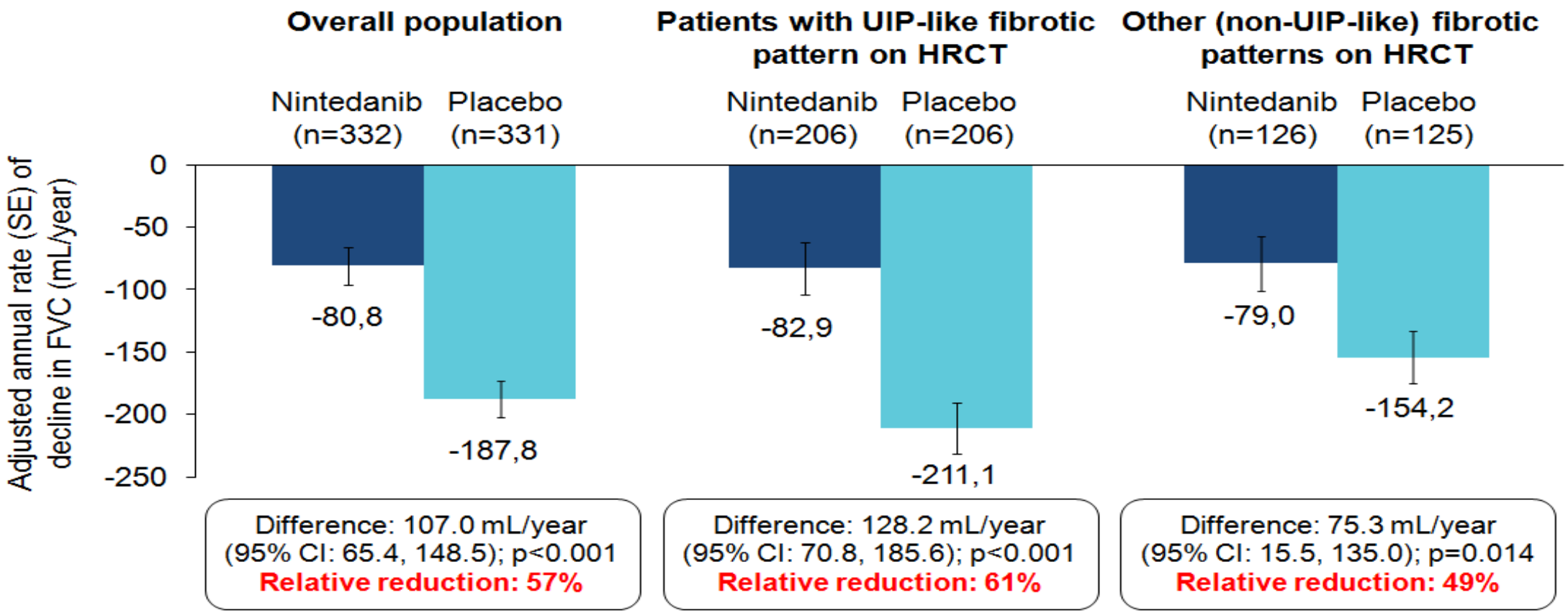
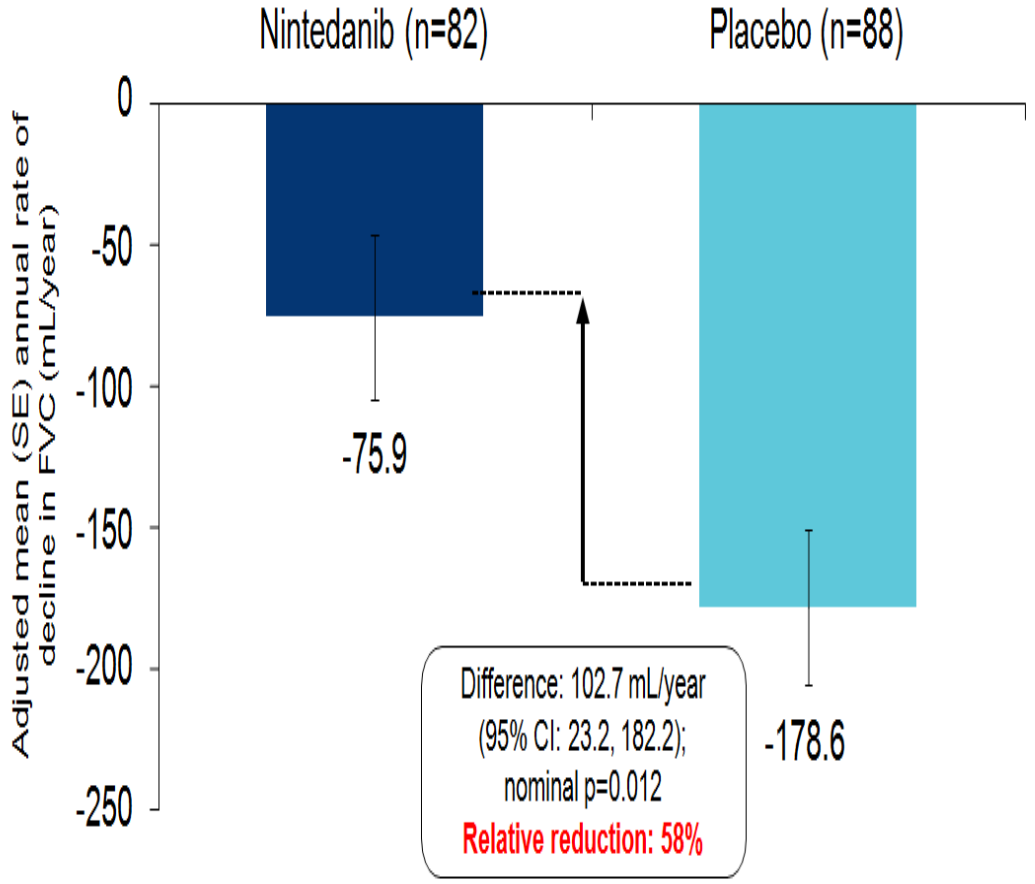


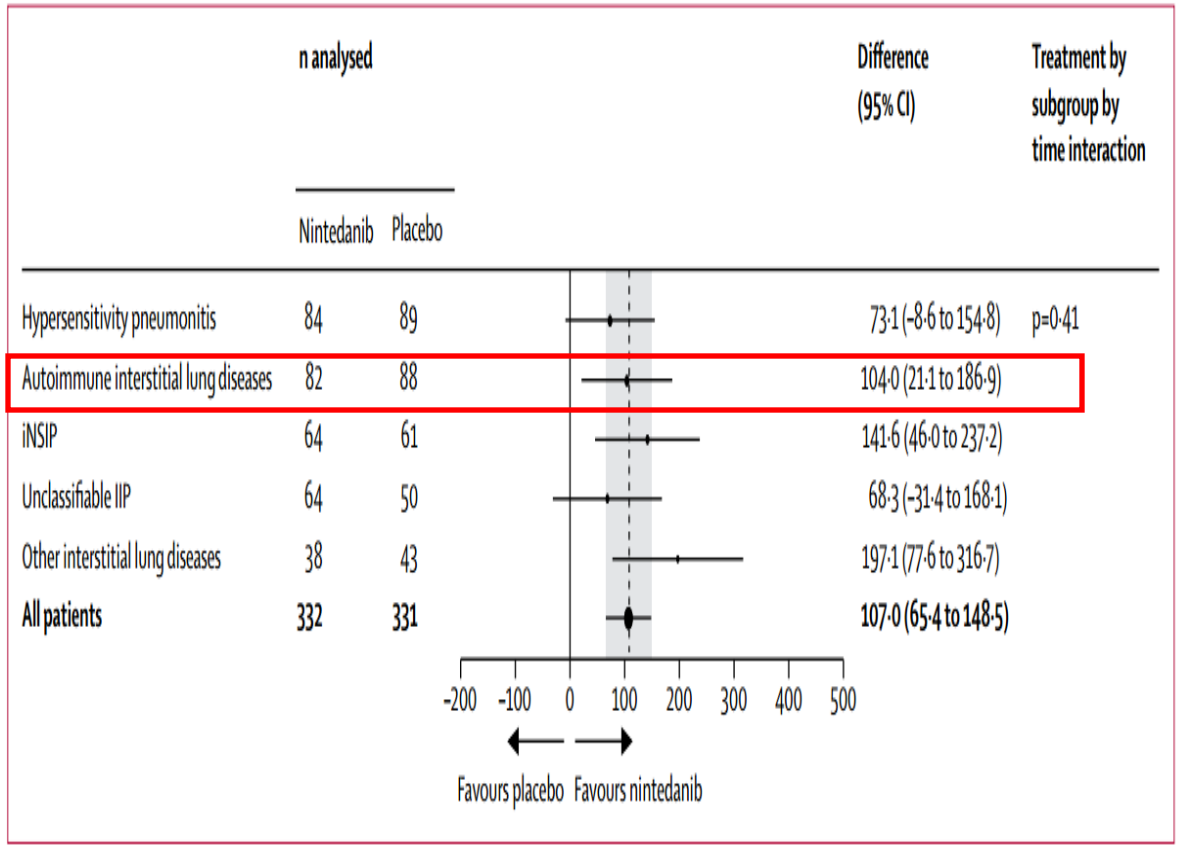
THE LANCET
Respiratory Medicine

# 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

2020;8: 453–60

*Athol U Wells, Kevin R Flaherty, Kevin K Brown, Yoshikazu Inoue, Anand Devaraj, Luca Richeldi, Teng Moua, Bruno Crestani, Wim A Wuyts, Susanne Stowasser, Manuel Quaresma, Rainer-Georg Goeldner, Rozsa Schlenker-Herceg, Martin Kolb on behalf of the INBUILD trial investigators**



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EUROPEAN CONGRESS OF RHEUMATOLOGY
2021 | 2–5 JUNE

# OP0124 EFFECTS OF NINTEDANIB IN PATIENTS WITH PROGRESSIVE FIBROSING INTERSTITIAL LUNG DISEASE ASSOCIATED WITH RHEUMATOID ARTHRITIS (RA-ILD) IN THE INBUILD TRIAL FREE

C. Kelly [1], E. Matteson [2], M. Aringer [3], G. R. Burmester [4], H. Mueller [5], L. Moros [6], K. Rohr [6], M. Kolb [7] on behalf of the INBUILD Trial Investigators.

| Baseline characteristic | Nintedanib (n=42) | Placebo (n=47) |
|---|---|---|
| Mean age (years) | 66.8 | 67.0 |
| Male, % | 59.5 | 61.7 |
| Mean time since RA diagnosis (years) | 10.1 | 9.8 |
| Former or current smoker, % | 66.7 | 61.7 |
| bDMARDs, % | 26.2 | 17.0 |
| Non-biologic DMARDs, % | 52.4 | 55.3 |
| Glucocorticoids, %* | 76.2 | 70.2 |

- Nintedanib reduced the rate of decline in FVC (mL/year) over 52 weeks in patients with RA-ILD (**Figure 1;** mean difference 116.7 mL [95% CI: 7.4, 226.1]; *P*=0.037); consistent with the effect observed in the overall INBUILD® trial population[2] (107.0 mL [95% CI: 65.4, 148.5]; *P*<0.001)

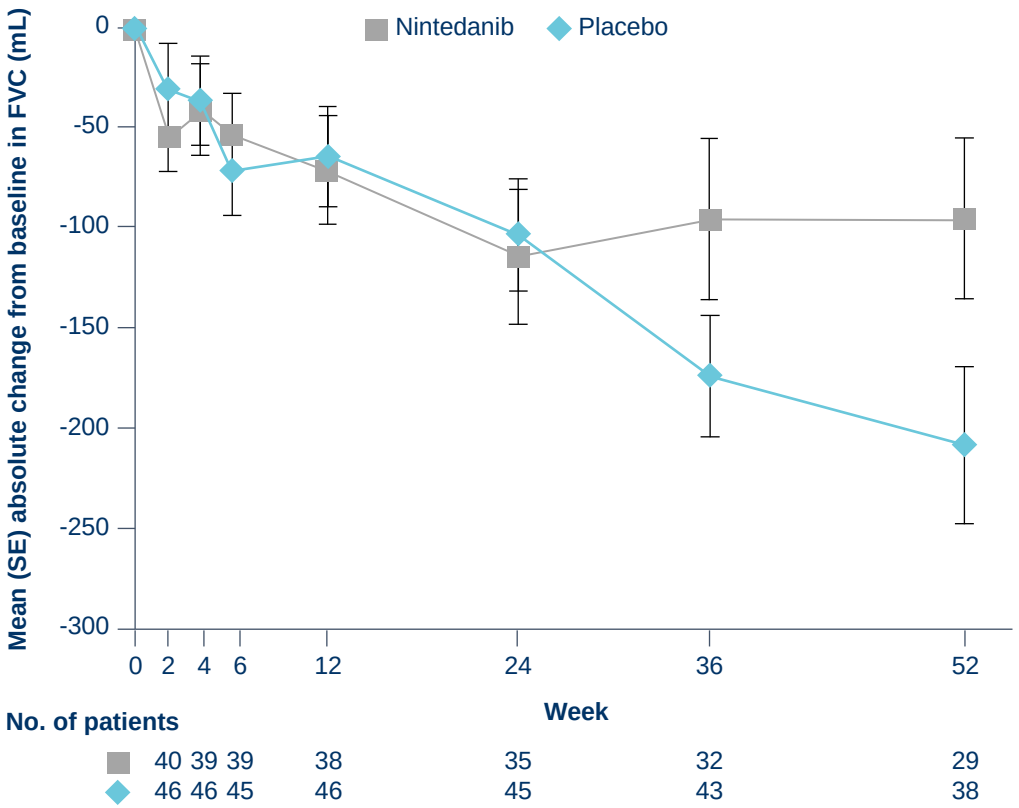



**Figure 1.** Absolute change from baseline in FVC (mL) at week 52 in patients with RA-ILD in the INBUILD® trial[1]

*≤20 mg/day prednisone or equivalent

1. Kelly C *et al*. EULAR European Congress of Rheumatology 2021. E-congress, June 2–5, 2021: OP0124; 2 Flaherty KR *et al. N Engl J Med* 2019;381:1718–27

RESEARCH Open Access

Respiratory Research

(2021) 22:84

# Nintedanib and immunomodulatory therapies in progressive fibrosing interstitial lung diseases

Vincent Cottin[1*], Luca Richeldi[2], Ivan Rosas[3], Maria Otaola[4], Jin Woo Song[5], Sara Tomassetti[6], Marlies Wijsenbeek[7], Manuela Schmitz[8], Carl Coeck[9], Susanne Stowasser[10], Rozsa Schlenker-Herceg[11] and Martin Kolb[12] on behalf of the INBUILD Trial Investigators

**Table 2** Restricted or prohibited immunomodulatory or antifibrotic therapies taken at baseline, during treatment with trial drug and/or following discontinuation of trial drug over 52 weeks by customized drug grouping or preferred name

| | Nintedanib (n = 332) | Placebo (n = 331) |
|---|---|---|
| ≥ 1 restricted or prohibited therapy | 53 (16.0) | 91 (27.5) |
| Glucocorticoids[a] | 44 (13.3) | 72 (21.8) |
| Mycophenolate mofetil | 9 (2.7) | 9 (2.7) |
| Azathioprine | 4 (1.2) | 6 (1.8) |
| Tacrolimus | 4 (1.2) | 5 (1.5) |
| Ciclosporin | 1 (0.3) | 6 (1.8) |
| Rituximab | 3 (0.9) | 2 (0.6) |
| Cyclophosphamide | 0 (0.0) | 3 (0.9) |
| Nintedanib[a] | 0 (0.0) | 3 (0.9) |
| Pirfenidone[a] | 2 (0.6) | 1 (0.3) |

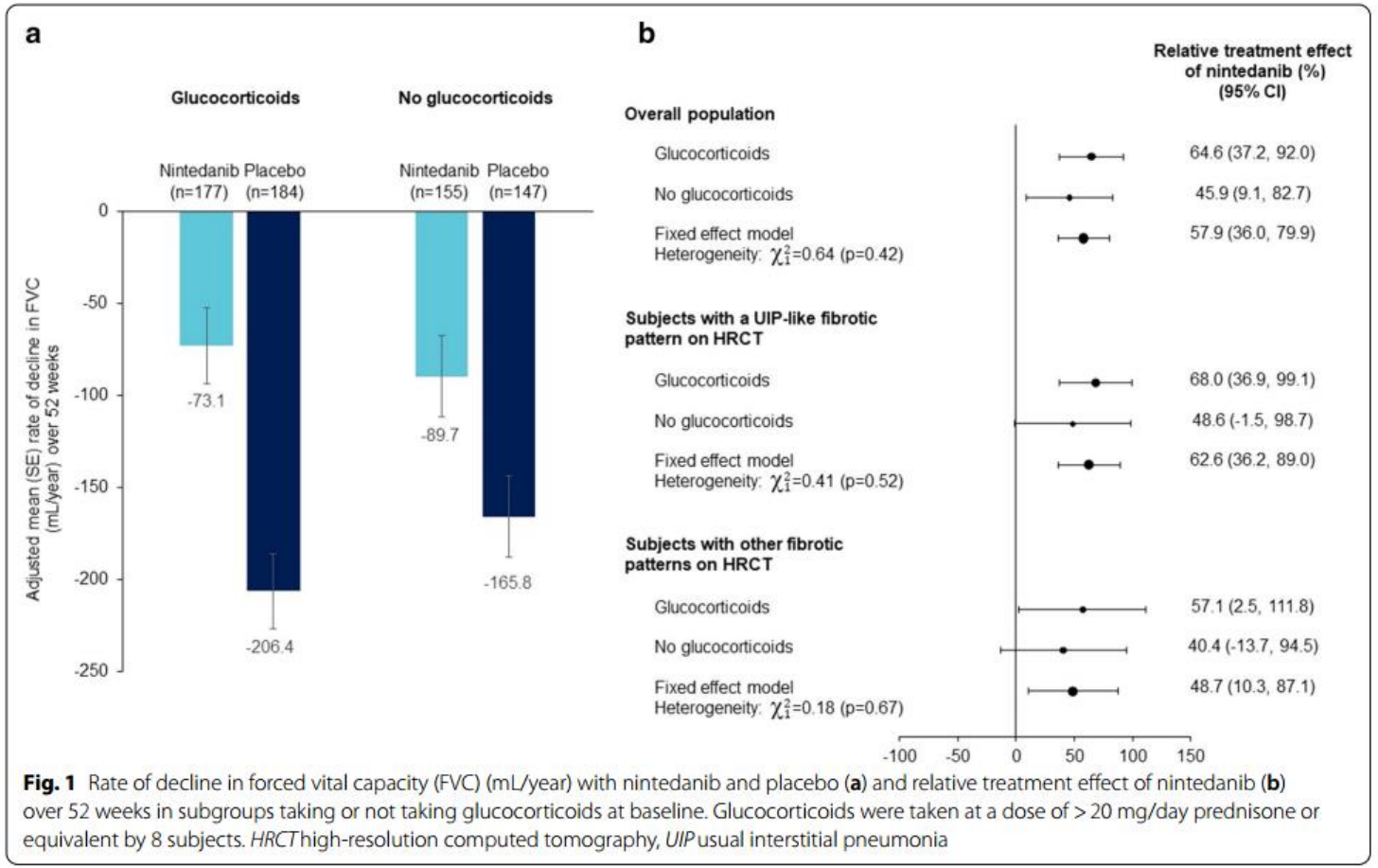



**Fig. 1** Rate of decline in forced vital capacity (FVC) (mL/year) with nintedanib and placebo (**a**) and relative treatment effect of nintedanib (**b**) over 52 weeks in subgroups taking or not taking glucocorticoids at baseline. Glucocorticoids were taken at a dose of > 20 mg/day prednisone or equivalent by 8 subjects. *HRCT* high-resolution computed tomography, *UIP* usual interstitial pneumonia

Respiratory Research

RESEARCH Open Access

# Nintedanib and immunomodulatory therapies in progressive fibrosing interstitial lung diseases

(2021) 22:84

Vincent Cottin[1*], Luca Richeldi[2], Ivan Rosas[3], Maria Otaola[4], Jin Woo Song[5], Sara Tomassetti[6], Marlies Wijsenbeek[7], Manuela Schmitz[8], Carl Coeck[9], Susanne Stowasser[10], Rozsa Schlenker-Herceg[11] and Martin Kolb[12] on behalf of the INBUILD Trial Investigators

**Table 3** Adverse events in subgroups by use of restricted or prohibited immunomodulatory or antifibrotic therapies

| | Restricted/prohibited medication use | | No restricted/prohibited medication use | |
|---|---|---|---|---|
| | Nintedanib (n = 39) | Placebo (n = 80) | Nintedanib (n = 293) | Placebo (n = 251) |
| Any adverse event | 39 (100.0) | 78 (97.5) | 278 (94.9) | 218 (86.9) |
| Most frequent adverse events[a] | | | | |
| Diarrhea | 27 (69.2) | 19 (23.8) | 195 (66.6) | 60 (23.9) |
| Nausea | 12 (30.8) | 10 (12.5) | 84 (28.7) | 21 (8.4) |
| Bronchitis | 14 (35.9) | 20 (25.0) | 27 (9.2) | 27 (10.8) |
| Nasopharyngitis | 3 (7.7) | 10 (12.5) | 41 (14.0) | 30 (12.0) |
| Dyspnea | 8 (20.5) | 19 (23.8) | 28 (9.6) | 25 (10.0) |
| Vomiting | 8 (20.5) | 3 (3.8) | 53 (18.1) | 14 (5.6) |
| Cough | 5 (12.8) | 16 (20.0) | 28 (9.6) | 28 (11.2) |
| Decreased appetite | 6 (15.4) | 6 (7.5) | 42 (14.3) | 11 (4.4) |
| Headache | 4 (10.3) | 9 (11.3) | 31 (10.6) | 14 (5.6) |
| Alanine aminotransferase increased | 6 (15.4) | 5 (6.3) | 37 (12.6) | 7 (2.8) |
| Progression of ILD[b] | 8 (20.5) | 25 (31.3) | 8 (2.7) | 14 (5.6) |
| Weight decreased | 4 (10.3) | 3 (3.8) | 37 (12.6) | 8 (3.2) |
| Aspartate aminotransferase increased | 6 (15.4) | 5 (6.3) | 32 (10.9) | 7 (2.8) |
| Abdominal pain | 3 (7.7) | 2 (2.5) | 31 (10.6) | 6 (2.4) |
| Serious adverse event[c] | 27 (69.2) | 45 (56.3) | 80 (27.3) | 65 (25.9) |
| Fatal adverse event | 3 (7.7) | 8 (10.0) | 8 (2.7) | 9 (3.6) |
| Adverse event leading to permanent treatment discontinuation | 8 (20.5) | 10 (12.5) | 57 (19.5) | 24 (9.6) |

While the INBUILD trial was not designed to evaluate the effects of concomitant medications

✓the use of immunomodulatory therapies at baseline or during the trial did not affect the benefit of nintedanib

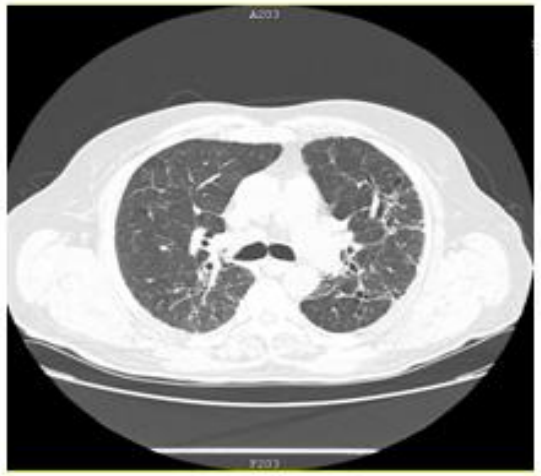
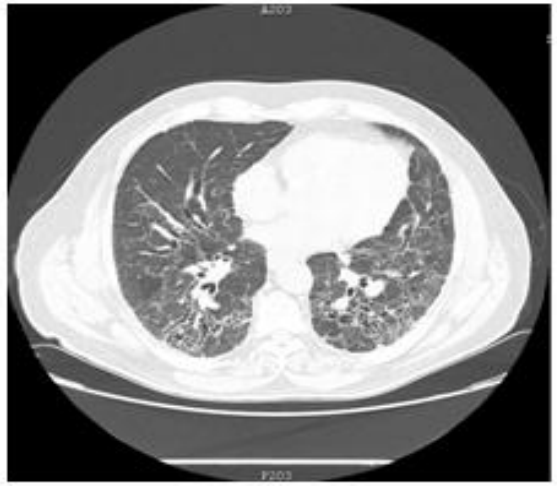
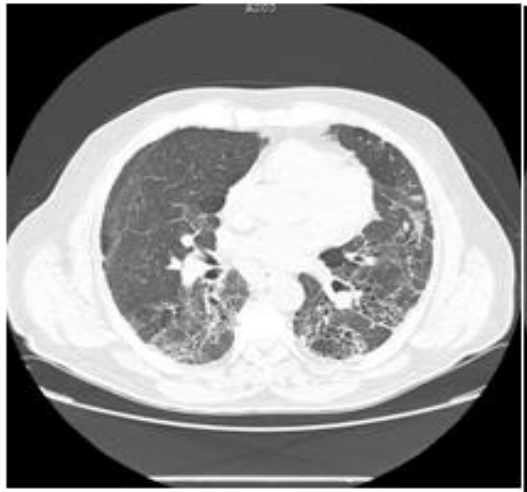
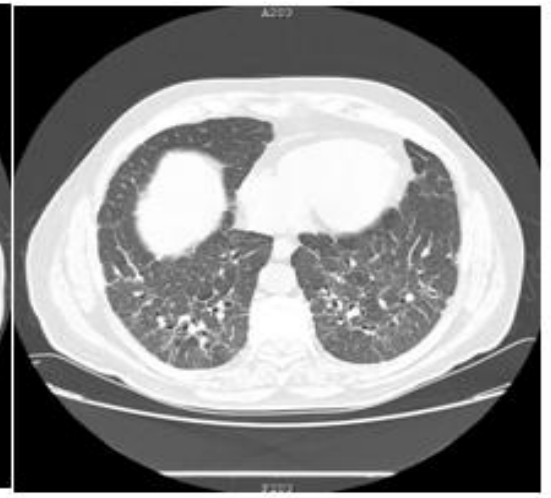
✓no safety issues regarding co-administration of immunomodulatory therapies and nintedanib

# CASE 1

Ασθενής άρρεν 60 ετών (RF, anti-ccp positive) RA από 10ετίας
Θεραπεία
-χαμηλές δόσεις κορτικοειδών
-MTX καλή ανταπόκριση – διακοπή λόγω δυσανεξίας γαστρεντερικού

Διάγνωση πνευμονικής ίνωσης 10/2017
(τρίζοντες βάσεων, ήπια δύσπνοια)
HRCT πνεύμονα: UIP
Έναρξη Rituximab
Prezolon 5 mg

| | 10/17 |
|---|---|
| | RTX |
| FVC | 70 |
| FEV1 | 76 |
| DLCO | 45 |

# CASE 1

Ασθενής άρρεν 60 ετών (RF, anti-ccp positive) RA από 10ετίας
Θεραπεία
-χαμηλές δόσεις κορτικοειδών
-MTX καλή ανταπόκριση – διακοπή λόγω δυσανεξίας γαστρεντερικού

Διάγνωση πνευμονικής ίνωσης 10/2017
(τρίζοντες βάσεων, ήπια δύσπνοια)
HRCT πνεύμονα: UIP
Έναρξη Rituximab
Prezolon 5 mg

ΔΥΣΠΝΟΙΑ ΣΤΗΝ ΚΟΠΩΣΗ

| | 10/17 | 9/19 |
|---|---|---|
| | RTX | NINTED |
| FVC(%predicted) | 70 | 62↓ |
| FEV1(%predicted) | 76 | 70↓ |
| DLCO(%predicted) | 45 | 40 |

Προσθήκη nintedanib 150mg 1x2

# CASE 1

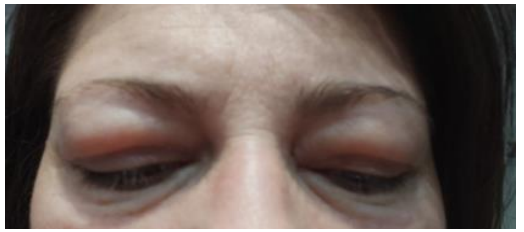
Ασθενής 60 ετών (RF, anti-ccp positive) RA από 10ετίας
Θεραπεία
-χαμηλές δόσεις κορτικοειδών
-MTX καλή ανταπόκριση – διακοπή λόγω δυσανεξίας γαστρεντερικού

Διάγνωση πνευμονικής ίνωσης 10/2017
(τρίζοντες βάσεων, ήπια δύσπνοια)
HRCT πνεύμονα: UIP
Rituximab
Prezolon 2,5 mg ↓
Nintedanib 150mg 1X2
Σταθερή λειτουργική κατάσταση NYHA II

| | 10/17 | 9/19 | 8/20 | 2/21 | 7/21 |
|---|---|---|---|---|---|
| | RTX | NINTED | | | |
| FVC(%predicted) | 70 | 62↓ | 75 | 78 | 76 |
| FEV1(%predicte) | 76 | 70↓ | 81 | 84 | 86 |
| DLCO(%predicte) | 45 | 40 | 44 | 38 | 34 |

# CASE 2

Ασθενής γυναίκα 54 ετών εμφανίζει προοδευτικά επιδεινούμενη δύσπνοια και ήπιο περιστασιακό εξάνθημα προσώπου οίδημα βλεφάρων, αρθραλγίες, πυρετική κίνηση?



Ατομικό ιστορικό ελεύθερο (υπερλιπιδαιμία, καπνίστρια)

Χορήγηση διαφόρων αντιβιοτικών χωρίς ανταπόκριση

Λόγω δύσπνοιας και χαμηλού κορεσμού O2 (86%) παραπομπή σε νοσοκομείο

CTPA: χωρίς εικόνα πνευμονικής εμβολής

HRCT: διηθήσεις θολής υάλου στις βάσεις αμφοτερόπλευρα, πύκνωση με αεροβροχόγραμμα στο έξω τμήμα του μέσω λοβού, γραμμοειδής και οζιδιακού τύπου διηθήσεις

BAL: (85% Λεμφοκύτταρα, αρνητικές καλλιέργειες για κόκκους (-) και P. Jirovecci(-)
Καλλιέργειες αίματος (-)

# CASE 2

Οξυγονοθεραπεία
Προωθημένες αντιβιοτικές αγωγές
Methylpred 1gr/kg IV

↑ ↑ ↑ Ανάγκες σε $O_2$ 6lt/min σε ηρεμία

| | |
|---|---|
| WBC | 13.400 (85% ΠΟΛΥ) |
| HB (gr/dl) | 11.2 |
| PLT/μl | 205.000 |
| URE(mg/dl) | 16 |
| CRE (mg/dl) | 0.79 |
| SGOT (U/L) | 35 |
| SGPT (U/L) | 40 |
| CHOL (U/L) | 6,5 |
| ALP (U/L) | 56 |
| ΛΕΥΚ (mg/dl) | 6,7 (3,2) |
| CPK (U/L) | 944 U/L |
| LDH | 475 U/L |
| φερριτίνη | 20 |
| ΤΚΕ (mm/h) | 35 |
| CRP (mg/dl) | 11,2(<5) |
| Γ. ΟΥΡΩΝ | κφ |

Οξυγονοθεραπεία
Προωθημένες αντιβιοτικές αγωγές
Methylpred 1gr/kg IV

↑ ↑ ↑ Ανάγκες σε $O_2$ 6lt/min σε ηρεμία

| | |
|---|---|
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| CRE (mg/dl) | 0.79 |
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| SGPT (U/L) | 40 |
| CHOL (U/L) | 6,5 |
| ALP (U/L) | 56 |
| ΛΕΥΚ (mg/dl) | 6,7 (3,2) |
| CPK (U/L) | 944 U/L |
| LDH | 475 U/L |
| φερριτίνη | 20 |
| ΤΚΕ (mm/h) | 35 |
| CRP (mg/dl) | 11,2(<5) |
| Γ. ΟΥΡΩΝ | κφ |

## ΣΥΝΔΡΟΜΟ ΑΝΤΙΣΥΝΘΕΤΑΣΗΣ – J0-1 ΘΕΤΙΚΟ

3ώσεις 1000mg methylprednisolone IV
1gr Endoxan IV

Βελτίωση κλινικής εικόνας

Εξιτήριο: Medrol 16mg 1x2
PPi, Calcioral, Bactrimel
$O_2$: 1lt/min μόνο κατά την κινητοποίηση

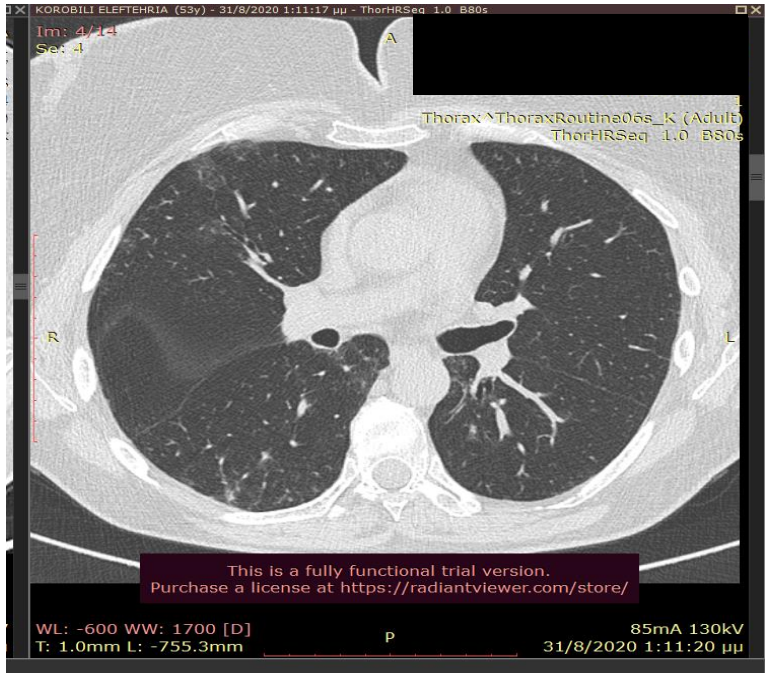
# CASE 2

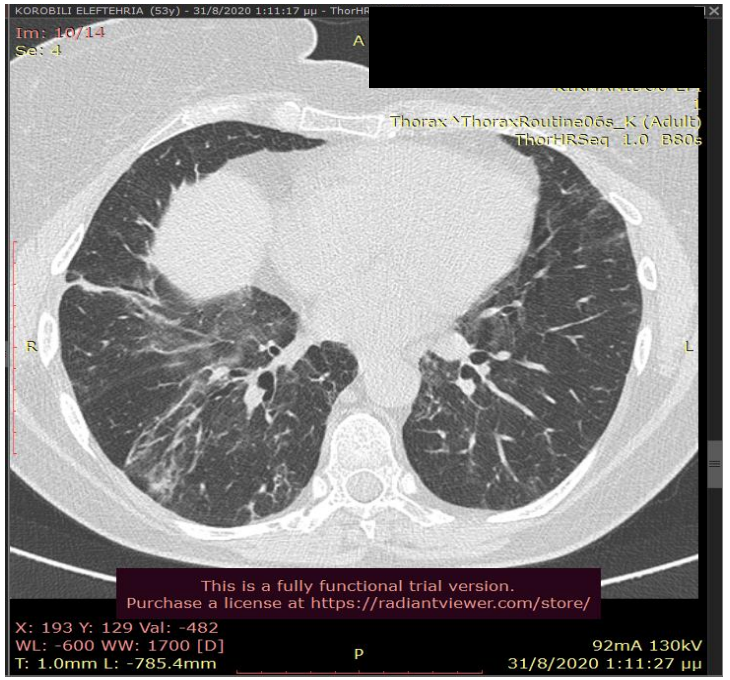
ΡΕΥΜΑΤΟΛΟΓΙΚΗ ΕΚΤΙΜΗΣΗ

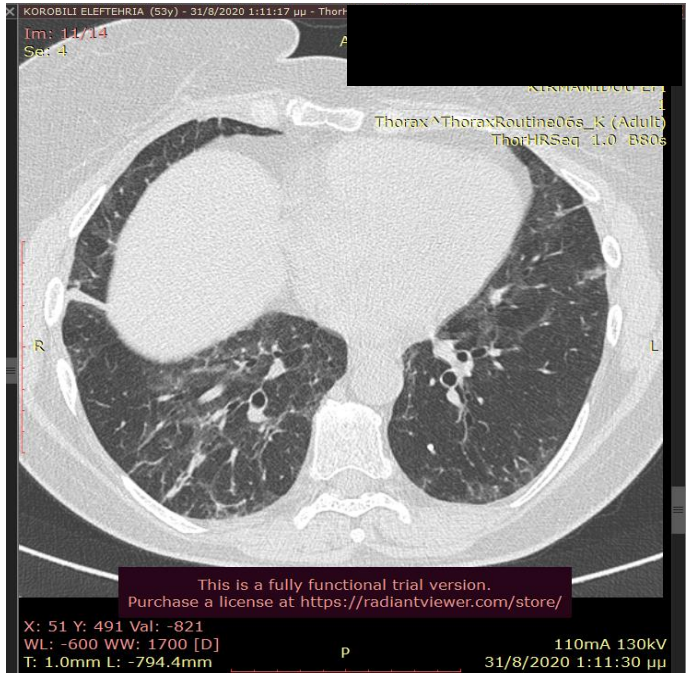
Συνέχιση μηνιαίων ώσεων ENDOXAN
Σταδιακή μείωση κορτικοειδών

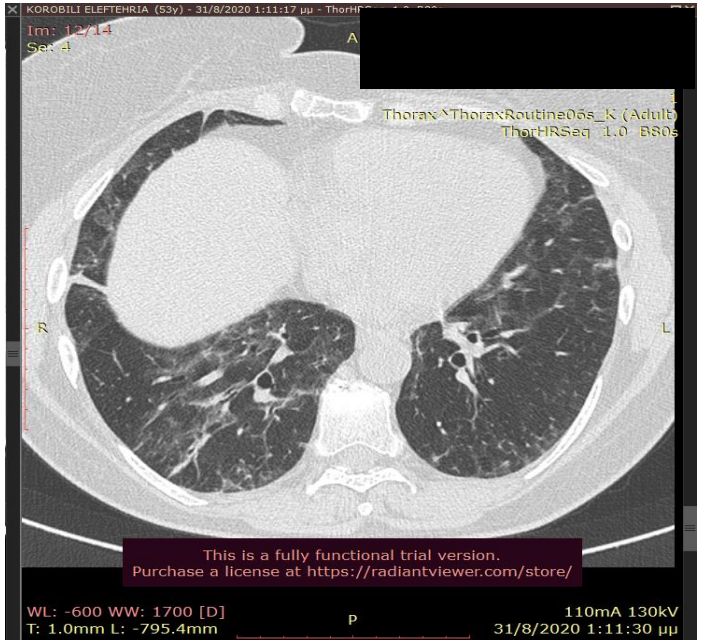
| | 7/20 | 8/20 |
|---|---|---|
| | | |
| FVC (% predicted) | 53 | 59 |
| FEV1 (% predicted) | 56 | 62 |
| DLCO (% predicted) | 43 | |

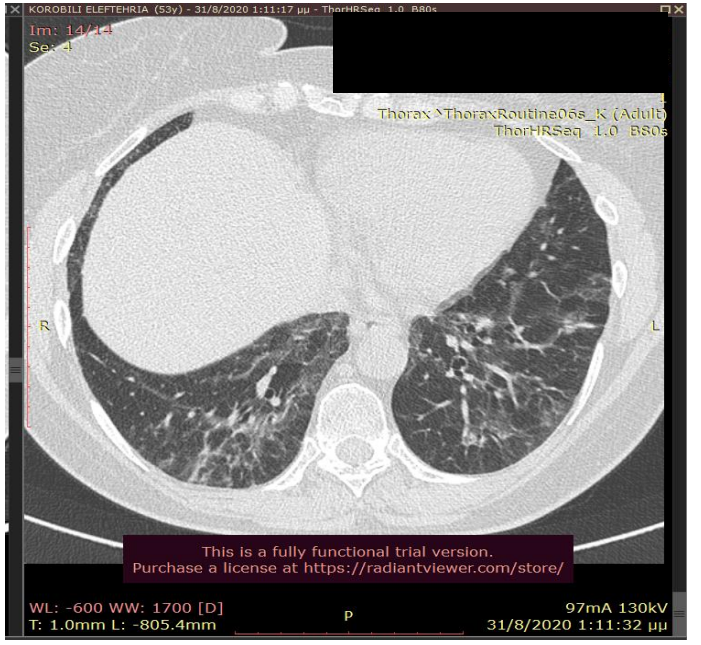
| | 7/20 | 9/20 |
|---|---|---|
| WBC | 13.400 (85% ΠΟΛΥ) | 8900 |
| HB (gr/dl) | 11.2 | 15,3 |
| PLT/μl | 205.000 | 276 |
| URE(mg/dl) | 16 | 23 |
| CRE (mg/dl) | 0.79 | 0,86 |
| SGOT (U/L) | 35 | 21 |
| SGPT (U/L) | 40 | 22 |
| ALP (U/L) | 56 | 78 |
| ΛΕΥΚ (mg/dl) | 6,7 (3,2) | 6.8(4,1) |
| CPK (U/L) | 944 U/L | 79 |
| LDH | 475 U/L | 245 |
| φερριτίνη | 20 | 34 |
| ΤΚΕ (mm/h) | 35 | 21 |
| CRP (mg/dl) | 11,2(<5) | 2 |
| Γ. ΟΥΡΩΝ | κφ | κφ |


KOROBILI ELEFTEHRIA (53y) - 31/8/2020 1:11:17 μμ - ThorHRSeq 1.0 B80s
Im: 4/14
Ser: 4
A
Thorax^ThoraxRoutine06s_K (Adult)
ThorHRSeq 1.0 B80s
R
L
This is a fully functional trial version.
Purchase a license at https://radiantviewer.com/store/
WL: -600 WW: 1700 [D]
T: 1.0mm L: -755.3mm
P
85mA 130kV
31/8/2020 1:11:20 μμ


Im: 10/14
Ser: 4
A
Thorax^ThoraxRoutine06s_K (Adult)
ThorHRSeq 1.0 B80s
R
L
This is a fully functional trial version.
Purchase a license at https://radiantviewer.com/store/
X: 193 Y: 129 Val: -482
WL: -600 WW: 1700 [D]
T: 1.0mm L: -785.4mm
P
92mA 130kV
31/8/2020 1:11:27 μμ


Im: 11/14
Ser: 4
Thorax^ThoraxRoutine06s_K (Adult)
ThorHRSeq 1.0 B80s
R
L
This is a fully functional trial version.
Purchase a license at https://radiantviewer.com/store/
X: 51 Y: 491 Val: -821
WL: -600 WW: 1700 [D]
T: 1.0mm L: -794.4mm
P
110mA 130kV
31/8/2020 1:11:30 μμ


Im: 12/14
Ser: 4
A
Thorax^ThoraxRoutine06s_K (Adult)
ThorHRSeq 1.0 B80s
R
L
This is a fully functional trial version.
Purchase a license at https://radiantviewer.com/store/
WL: -600 WW: 1700 [D]
T: 1.0mm L: -795.4mm
P
110mA 130kV
31/8/2020 1:11:30 μμ


KOROBILI ELEFTEHRIA (53y) - 31/8/2020 1:11:17 μμ - ThorHRSeq 1.0 B80s
Im: 14/14
Ser: 4
Thorax^ThoraxRoutine06s_K (Adult)
ThorHRSeq 1.0 B80s
R
L
This is a fully functional trial version.
Purchase a license at https://radiantviewer.com/store/
WL: -600 WW: 1700 [D]
T: 1.0mm L: -805.4mm
P
97mA 130kV
31/8/2020 1:11:32 μμ

ΡΕΥΜΑΤΟΛΟΓΙΚΗ ΕΚΤΙΜΗΣΗ

Συνέχιση μηνιαίων ώσεων ENDOXAN
Σταδιακή μείωση κορτικοειδών

| | 7/20 | 8/20 |
|---|---|---|
| | | NINTED |
| FVC (% predicted) | 53 | 59 |
| FEV1 (% predicted) | 56 | 62 |
| DLCO (% predicted) | 43 | |

Προσθήκη Nintedanib 150mg 1x2

| | 7/20 | 8/20 |
|---|---|---|
| WBC | 13.400 (85% ΠΟΛΥ) | 8900 |
| HB (gr/dl) | 11.2 | 15,3 |
| PLT/μl | 205.000 | 276 |
| URE(mg/dl) | 16 | 23 |
| CRE (mg/dl) | 0.79 | 0,86 |
| SGOT (U/L) | 35 | 21 |
| SGPT (U/L) | 40 | 22 |
| ALP (U/L) | 56 | 78 |
| ΛΕΥΚ (mg/dl) | 6,7 (3,2) | 6.8(4,1) |
| CPK (U/L) | 944 U/L | 79 |
| LDH | 475 U/L | 245 |
| φερριτίνη | 20 | 34 |
| ΤΚΕ (mm/h) | 35 | 21 |
| CRP (mg/dl) | 11,2(<5) | 2 |
| Γ. ΟΥΡΩΝ | κφ | κφ |

ΠΟΡΕΙΑ ΝΟΣΟΥ

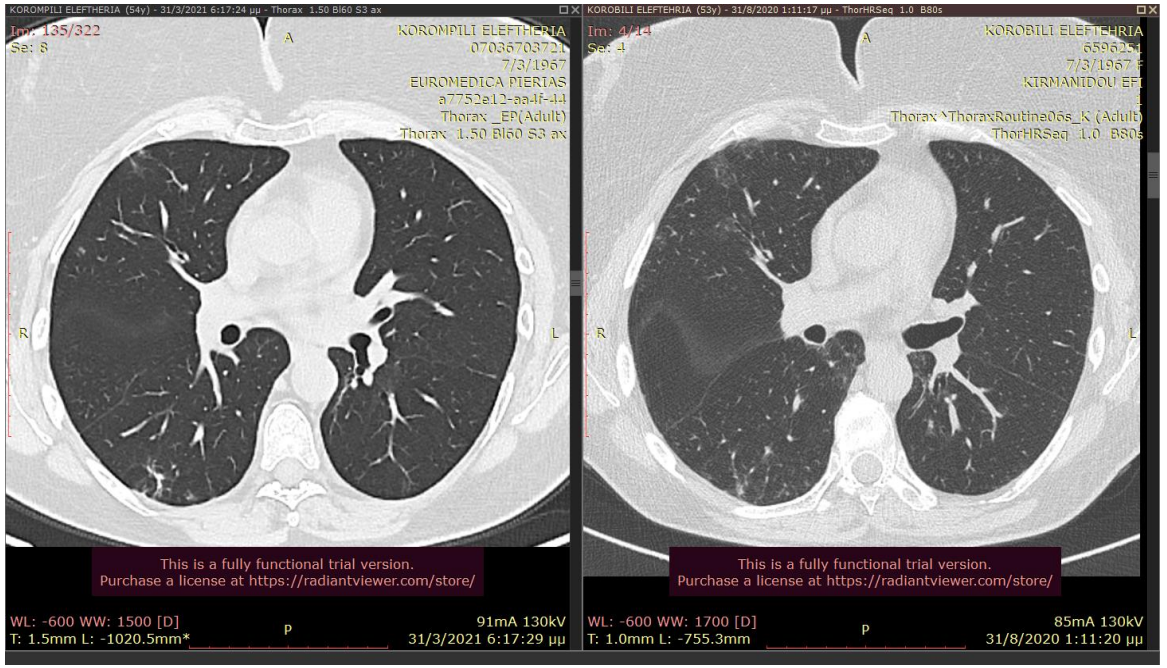
Ολοκλήρωση σχήματος Endoxan

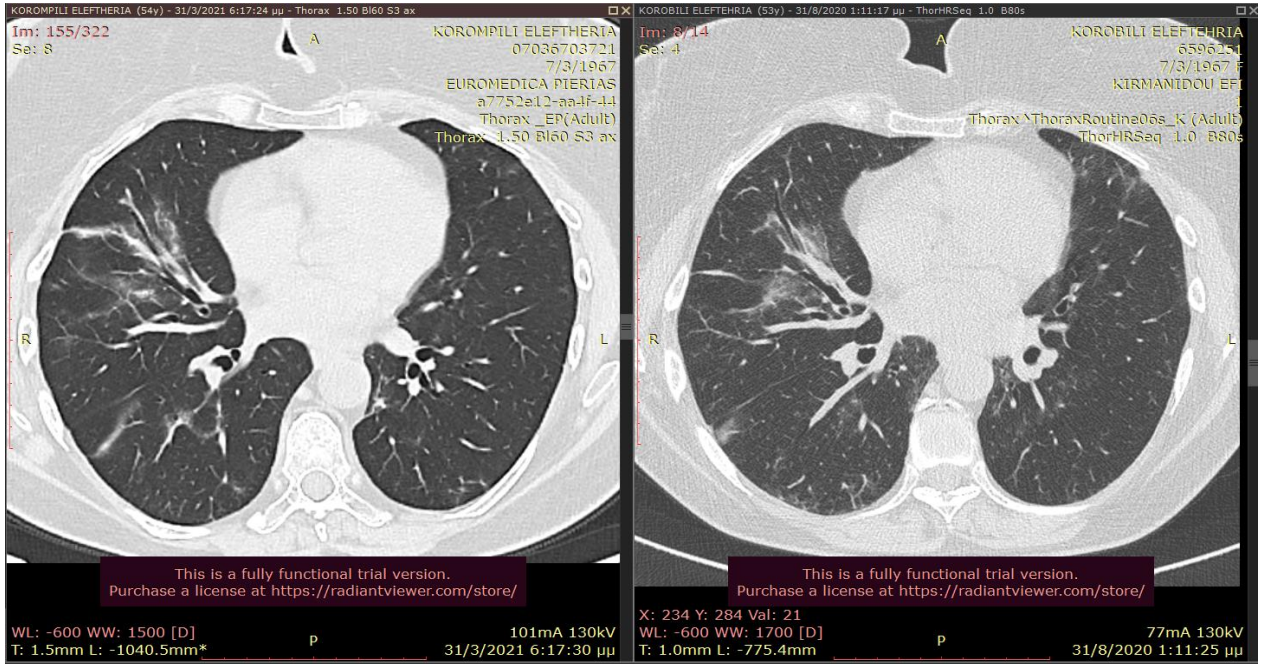
Έναρξη MMF 500mg 2x2

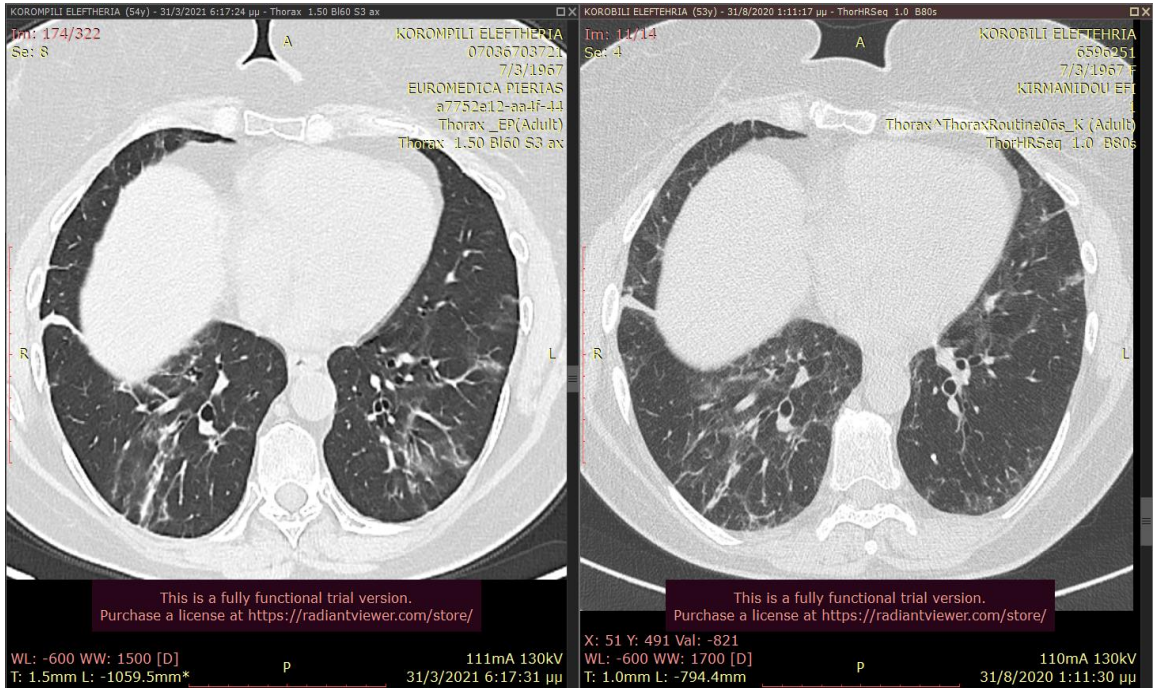
Συνέχιση Nintedanib 150mg 1x1 (ναυτία, έμετοι)

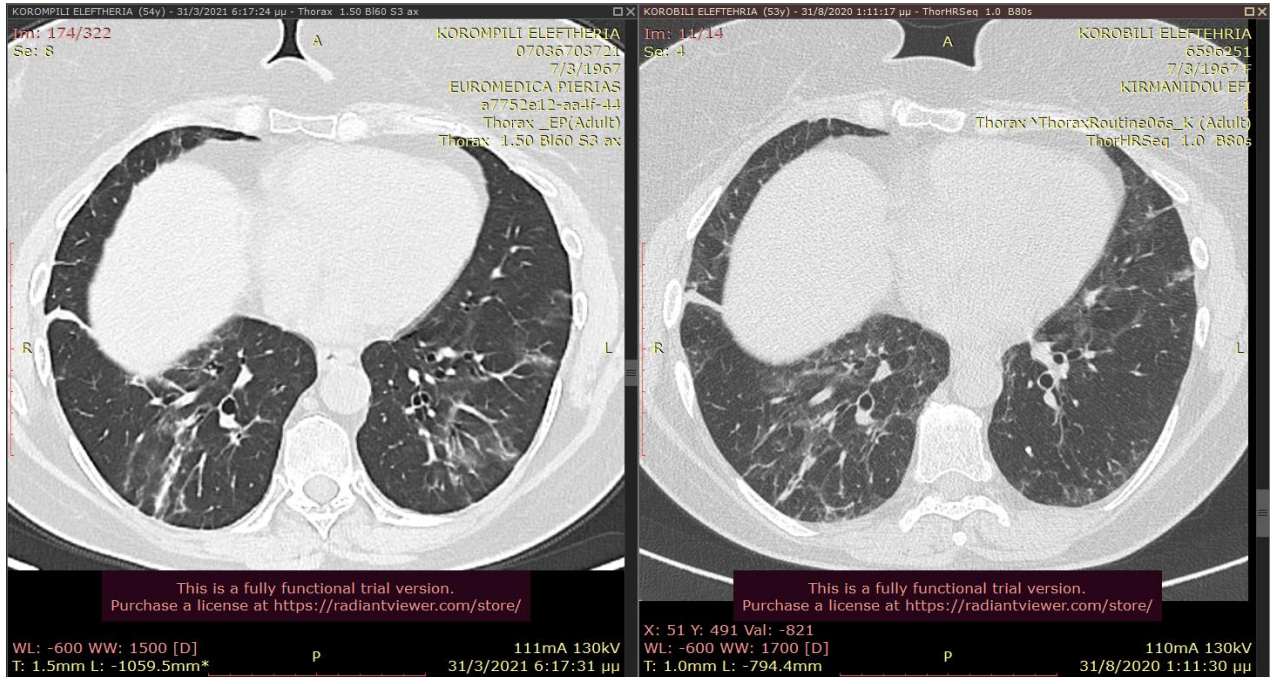
| | 7/20 | 8/20 | 1/21 |
|---|---|---|---|
| | | NINTED | |
| FVC (% predicted) | 53 | 59 | 64 |
| FEV1 (% predicted) | 56 | 62 | 71 |
| DLCO (% predicted) | 43 | | 68 |

Μεγάλη βελτίωση λειτουργικής ικανότητας
(χαμηλής έντασης άθληση, ποδήλατο κτλ)


KOROMPILI ELEFTHERIA (54y) - 31/3/2021 6:17:24 μμ - Thorax 1.50 Bl60 S3 ax
Im: 135/322
Se: 8
KOROMPILI ELEFTHERIA
07036703721
7/3/1967
EUROMEDICA PIERIAS
a7752e12-aa4f-44
Thorax _EP(Adult)
Thorax 1.50 Bl60 S3 ax
This is a fully functional trial version.
Purchase a license at https://radiantviewer.com/store/
WL: -600 WW: 1500 [D]
T: 1.5mm L: -1020.5mm*
91mA 130kV
31/3/2021 6:17:29 μμ
KOROBILI ELEFTEHRIA (53y) - 31/8/2020 1:11:17 μμ - ThorHRSeq 1.0 B80s
Im: 4/14
Se: 4
KOROBILI ELEFTEHRIA
6596251
7/3/1967 F
KIRMANIDOU EFI
Thorax ^ThoraxRoutine06s_K (Adult)
ThorHRSeq 1.0 B80s
This is a fully functional trial version.
Purchase a license at https://radiantviewer.com/store/
WL: -600 WW: 1700 [D]
T: 1.0mm L: -755.3mm
85mA 130kV
31/8/2020 1:11:20 μμ


KOROMPILI ELEFTHERIA (54y) - 31/3/2021 6:17:24 μμ - Thorax 1.50 Bl60 S3 ax
Im: 155/322
Se: 8
KOROMPILI ELEFTHERIA
07036703721
7/3/1967
EUROMEDICA PIERIAS
a7752e12-aa4f-44
Thorax _EP(Adult)
Thorax 1.50 Bl60 S3 ax
This is a fully functional trial version.
Purchase a license at https://radiantviewer.com/store/
WL: -600 WW: 1500 [D]
T: 1.5mm L: -1040.5mm*
101mA 130kV
31/3/2021 6:17:30 μμ
KOROBILI ELEFTEHRIA (53y) - 31/8/2020 1:11:17 μμ - ThorHRSeq 1.0 B80s
Im: 8/14
Se: 4
KOROBILI ELEFTEHRIA
6596251
7/3/1967 F
KIRMANIDOU EFI
Thorax ^ThoraxRoutine06s_K (Adult)
ThorHRSeq 1.0 B80s
This is a fully functional trial version.
Purchase a license at https://radiantviewer.com/store/
X: 234 Y: 284 Val: 21
WL: -600 WW: 1700 [D]
T: 1.0mm L: -775.4mm
77mA 130kV
31/8/2020 1:11:25 μμ


KOROMPILI ELEFTHERIA (54y) - 31/3/2021 6:17:24 μμ - Thorax 1.50 Bl60 S3 ax
Im: 174/322
Se: 8
KOROMPILI ELEFTHERIA
07036703721
7/3/1967
EUROMEDICA PIERIAS
a7752e12-aa4f-44
Thorax _EP(Adult)
Thorax 1.50 Bl60 S3 ax
This is a fully functional trial version.
Purchase a license at https://radiantviewer.com/store/
WL: -600 WW: 1500 [D]
T: 1.5mm L: -1059.5mm*
111mA 130kV
31/3/2021 6:17:31 μμ
KOROBILI ELEFTEHRIA (53y) - 31/8/2020 1:11:17 μμ - ThorHRSeq 1.0 B80s
Im: 11/14
Se: 4
KOROBILI ELEFTEHRIA
6596251
7/3/1967 F
KIRMANIDOU EFI
Thorax ^ThoraxRoutine06s_K (Adult)
ThorHRSeq 1.0 B80s
This is a fully functional trial version.
Purchase a license at https://radiantviewer.com/store/
X: 51 Y: 491 Val: -821
WL: -600 WW: 1700 [D]
T: 1.0mm L: -794.4mm
110mA 130kV
31/8/2020 1:11:30 μμ


KOROMPILI ELEFTHERIA (54y) - 31/3/2021 6:17:24 μμ - Thorax 1.50 Bl60 S3 ax
Im: 174/322
Se: 8
KOROMPILI ELEFTHERIA
07036703721
7/3/1967
EUROMEDICA PIERIAS
a7752e12-aa4f-44
Thorax _EP(Adult)
Thorax 1.50 Bl60 S3 ax
This is a fully functional trial version.
Purchase a license at https://radiantviewer.com/store/
WL: -600 WW: 1500 [D]
T: 1.5mm L: -1059.5mm*
111mA 130kV
31/3/2021 6:17:31 μμ
KOROBILI ELEFTEHRIA (53y) - 31/8/2020 1:11:17 μμ - ThorHRSeq 1.0 B80s
Im: 11/14
Se: 4
KOROBILI ELEFTEHRIA
6596251
7/3/1967 F
KIRMANIDOU EFI
Thorax ^ThoraxRoutine06s_K (Adult)
ThorHRSeq 1.0 B80s
This is a fully functional trial version.
Purchase a license at https://radiantviewer.com/store/
X: 51 Y: 491 Val: -821
WL: -600 WW: 1700 [D]
T: 1.0mm L: -794.4mm
110mA 130kV
31/8/2020 1:11:30 μμ

ΠΟΡΕΙΑ ΝΟΣΟΥ

Ολοκλήρωση σχήματος Endoxan

Έναρξη MMF 500mg 2x2

Συνέχιση Nintedanib 150mg 1x1 (ναυτία, έμετοι)

Medrol 2mg/day

Μεγάλη βελτίωση λειτουργικής ικανότητας
(χαμηλής έντασης άθληση, ποδήλατο κτλ)

| | 7/20 | 8/20 | 1/21 |
|---|---|---|---|
| | | NINTED | |
| FVC (% predicted) | 53 | 59 | 64 |
| FEV1 (% predicted) | 56 | 62 | 71 |
| DLCO (% predicted) | 43 | | 68 |

Συνέχιση αγωγής με Nintedanib - τροποποίηση δόσης 100mg 1X2

# ΣΥΜΠΕΡΑΣΜΑΤΑ

Η πνευμονική ίνωση στα συστηματικά νοσήματα αποτελεί αποτελεί σοβαρή επιπλοκή, με δυσμενή πρόγνωση και περιορισμένες θεραπευτικές επιλογές

Η καλύτερη κατανόηση των παθοφυσιολογικών μηχανισμών της πνευμονικής ίνωσης στα συστηματικά αυτοάνοσα νοσήματα έχει οδηγήσει σε νέες θεραπευτικές προσεγγίσεις που στοχεύουν τόσο στην ανοσολογική ενεργοποίηση αλλά και στην ινωτική εξεργασία

Το nintedanib είναι το πρώτο αντιϊνωτικό σκεύασμα που έχει δείξει σε τυχαιοποιημένες μελέτες ότι επιβραδύνει σημαντικά το ρυθμό εξέλιξης της πνευμονικής ίνωσης σε ένα ευρύ φάσμα συστηματικών νοσημάτων

Η συνχορήγηση ανοσοκατασταλτικής αγωγής και nintedanib φαίνεται να αποτελεί ασφαλή και αποτελεσματική επιλογή για τους ασθενείς με συστηματικά νοσήματα και πνευμονική ίνωση