

Emerging treatments for ILD and ongoing clinical trials

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Disclosures

- Consultancy fees from Brainomix Ltd
- Honoraria from Deep Health Ltd
- Investigator initiated study with Boehringer Ingelheim

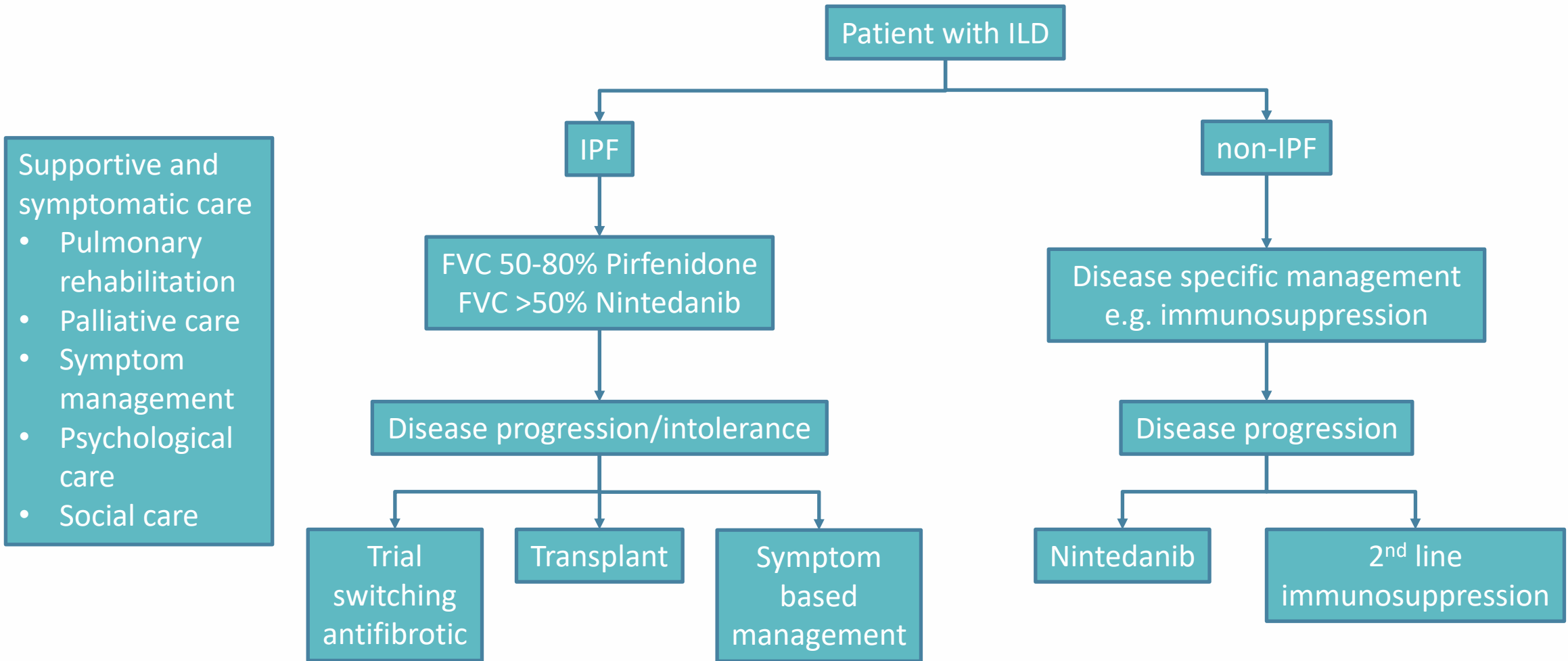


Outline

- Current ILD care in the UK
- New treatments for idiopathic pulmonary fibrosis and progressive pulmonary fibrosis
- New treatments for PH-ILD (*in brief*)
- Clinical trials in other ILD
- Clinical trials in systemic autoimmune rheumatic disease – ILD
- Symptomatic management of patients with ILD

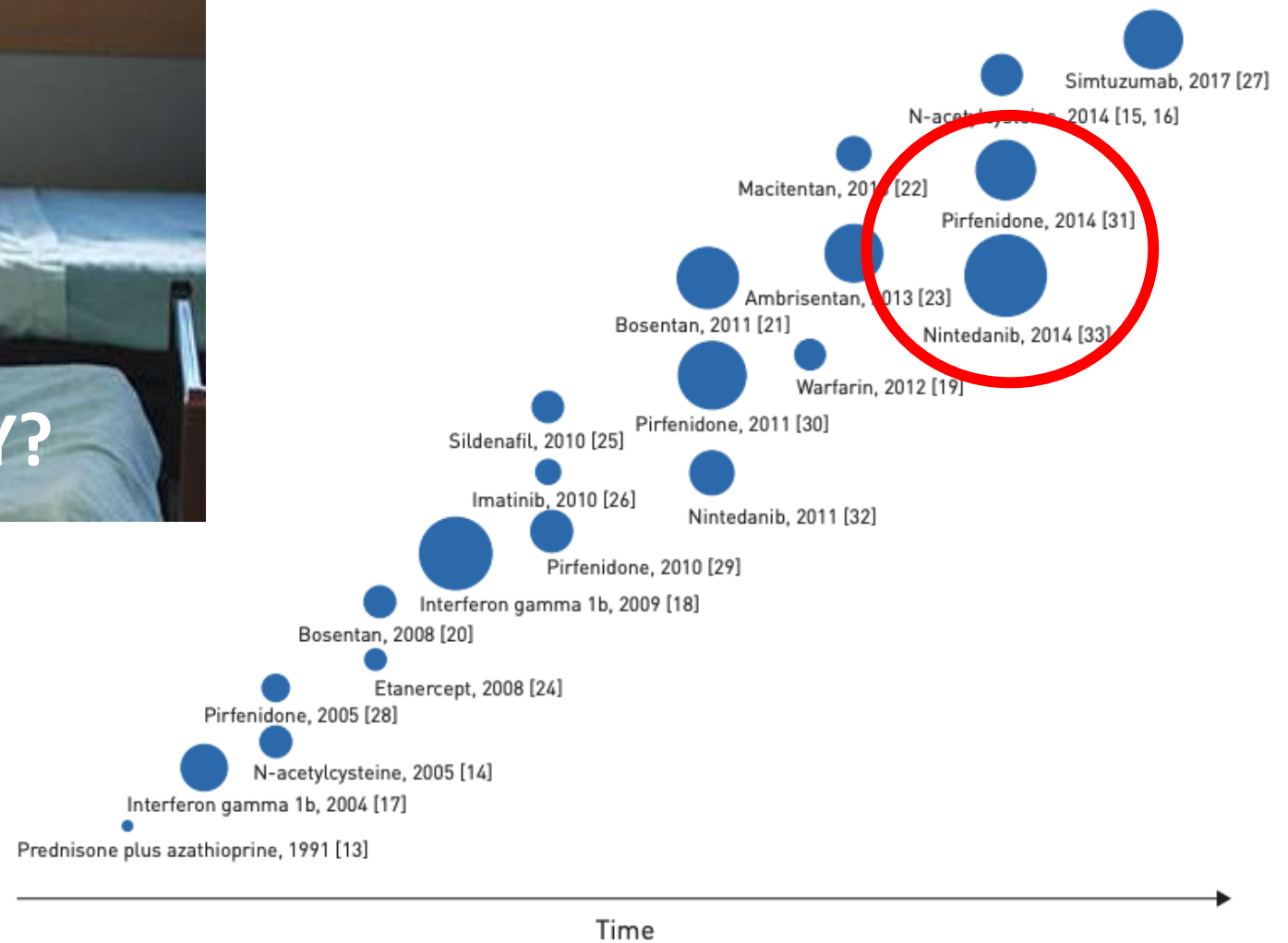


How do we currently manage ILD in the UK?





WHY ARE YOU SO GLOOMY?





Nintedanib (PPF), 2019

Nerandomilast IPF and PPF, 2025

Treprostinil, 2026

Mosliciguat (Phocus)
PH-ILD - 2

N-Acetylcysteine
(PRECISIONS-IPF) -
3

Admilparent (ALOFT)
PPF and IPF - 3

Belimumab in SSc-ILD
(BEconneCTD-ILD)

Inhaled pirfenidone (MIST) – 2b

Taladegib, (WHISTLE-
PF) – 2b

- Prednisolone in fHP (CHORUS)
- Lansoprazole in IPF (TIPAL)
- Metformin in IPF (MAVRIC)

Time



FIBRONEER-IPF – Trial design

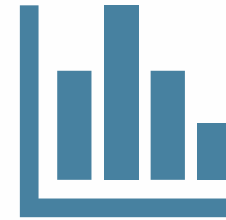


1117 patients with IPF



Nerandomilast 18mg or
9mg BD

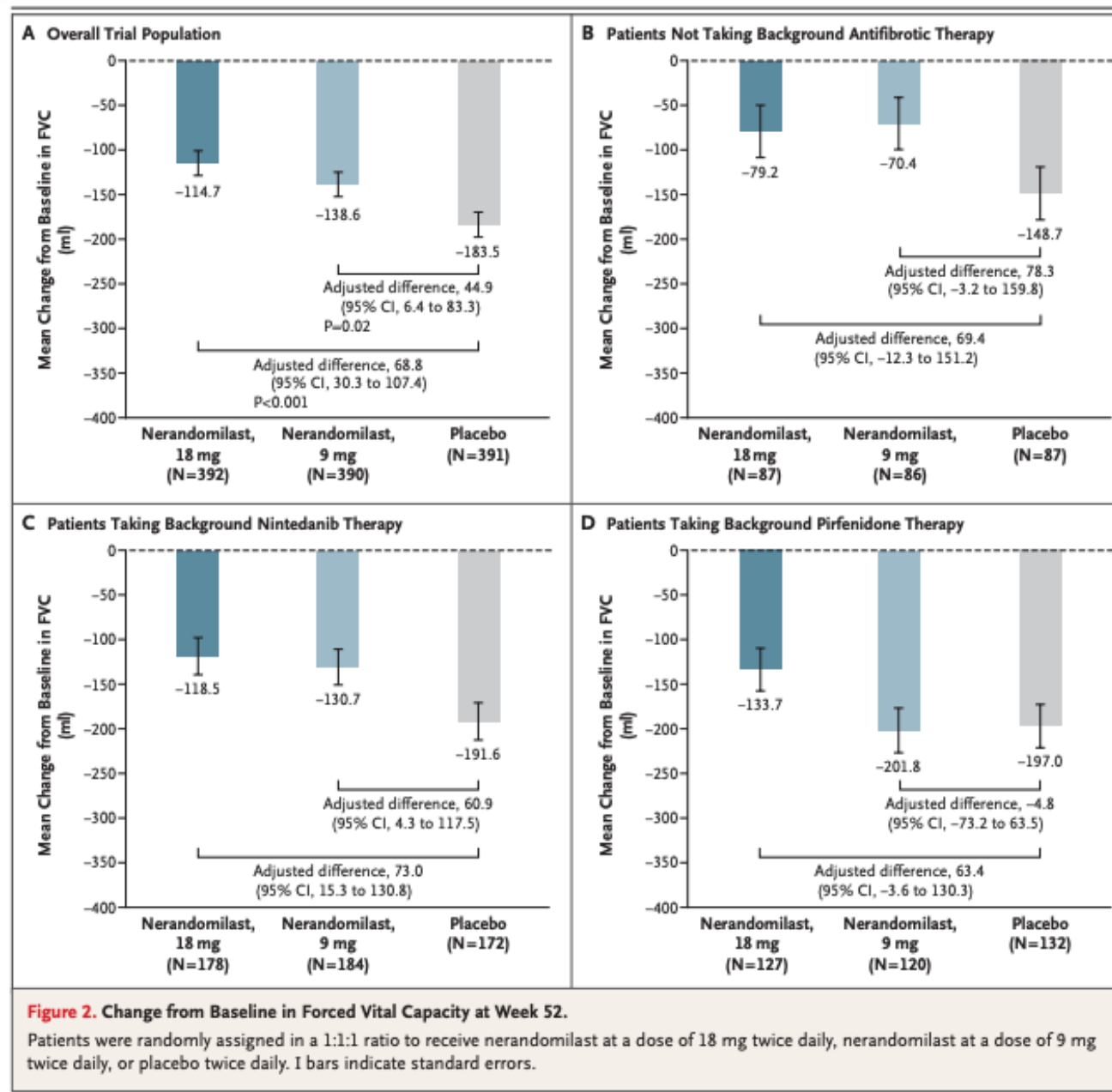
- Phosphodiesterase 4B inhibitor
- Anti-inflammatory and anti-fibrotic effects



12 months
Randomised

- 18mg BD vs 9 mg BD vs placebo
- Stratified to nintedanib or pirfenidone vs none

FIBRONEER- IPF Results



FIBRONEER-IPF – Adverse effects

	Placebo (n=393)	Nerandomilast 9 mg bd (n=392)	Nerandomilast 18 mg bd (n=392)
Diarrhea	72 (18.3)	126 (32.1)	166 (42.4)
COVID-19	57 (14.5)	73 (18.6)	57 (14.5)
Cough	74 (18.8)	72 (18.4)	68 (17.4)
Dyspnea	63 (16.0)	51 (13.0)	42 (10.7)
Upper respiratory tract infection	44 (11.2)	46 (11.7)	56 (14.3)
Nasopharyngitis	50 (12.7)	44 (11.2)	45 (11.5)
Condition aggravated	52 (13.2)	39 (10.0)	45 (11.5)
Weight decreased	38 (9.7)	43 (11.0)	48 (12.2)
Decreased appetite	27 (6.9)	38 (9.7)	40 (10.2)

FIBRONEER-ILD – Trial design



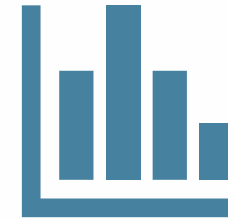
1176 patients with PPF

- Autoimmune ILD
- Hypersensitivity pneumonitis
- Unclassifiable
- Idiopathic NSIP



Nerandomilast 18mg or 9mg BD

- Phosphodiesterase 4B inhibitor
- Anti-inflammatory and anti-fibrotic effects

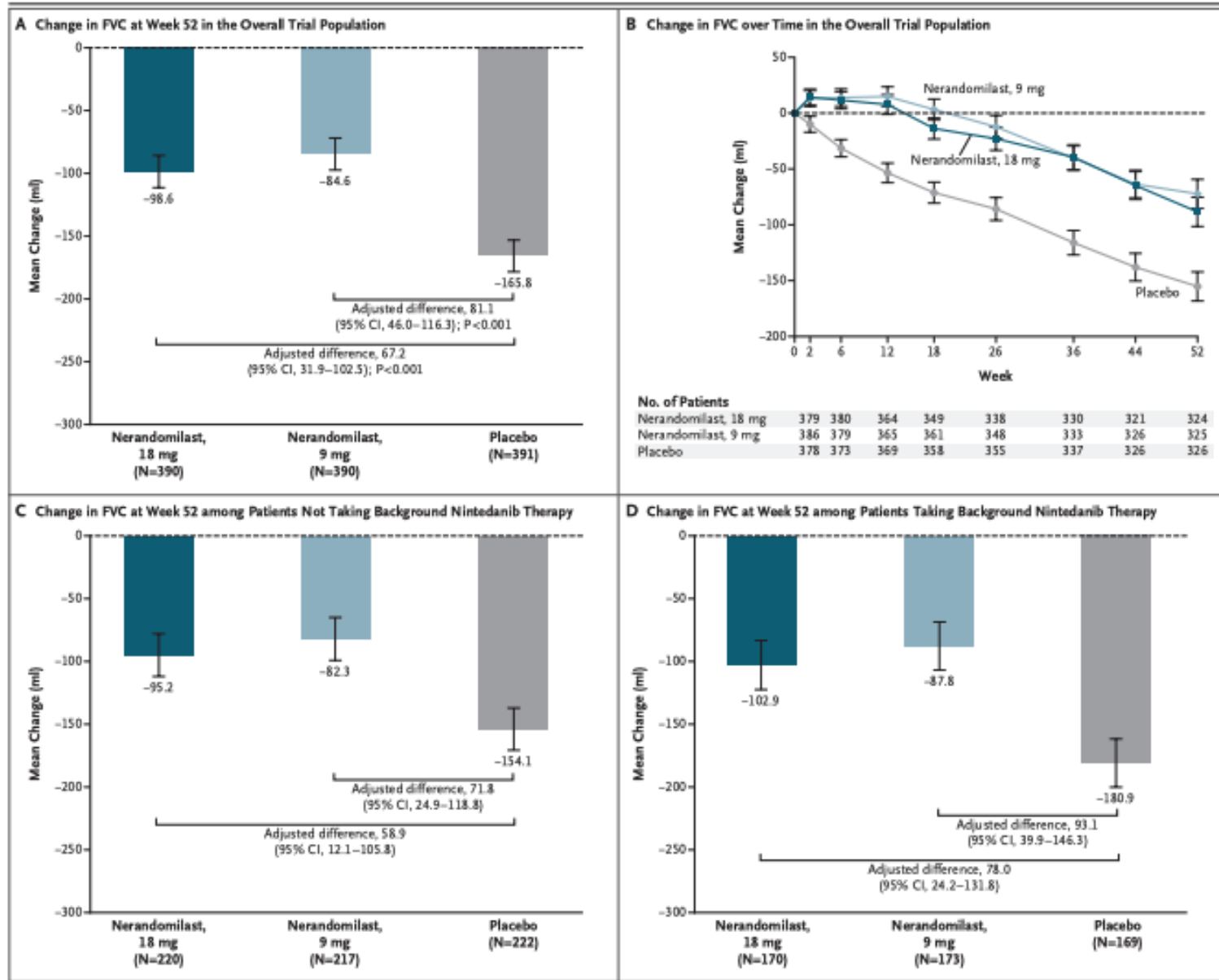


12 months

Randomised

- 18mg BD vs 9 mg BD vs placebo
- Stratified to nintedanib or none
- Excluded baseline cyclophosphamide, MMF, Pred >15mg

FIBRONEER- ILD Results



Nerandomilast in the UK

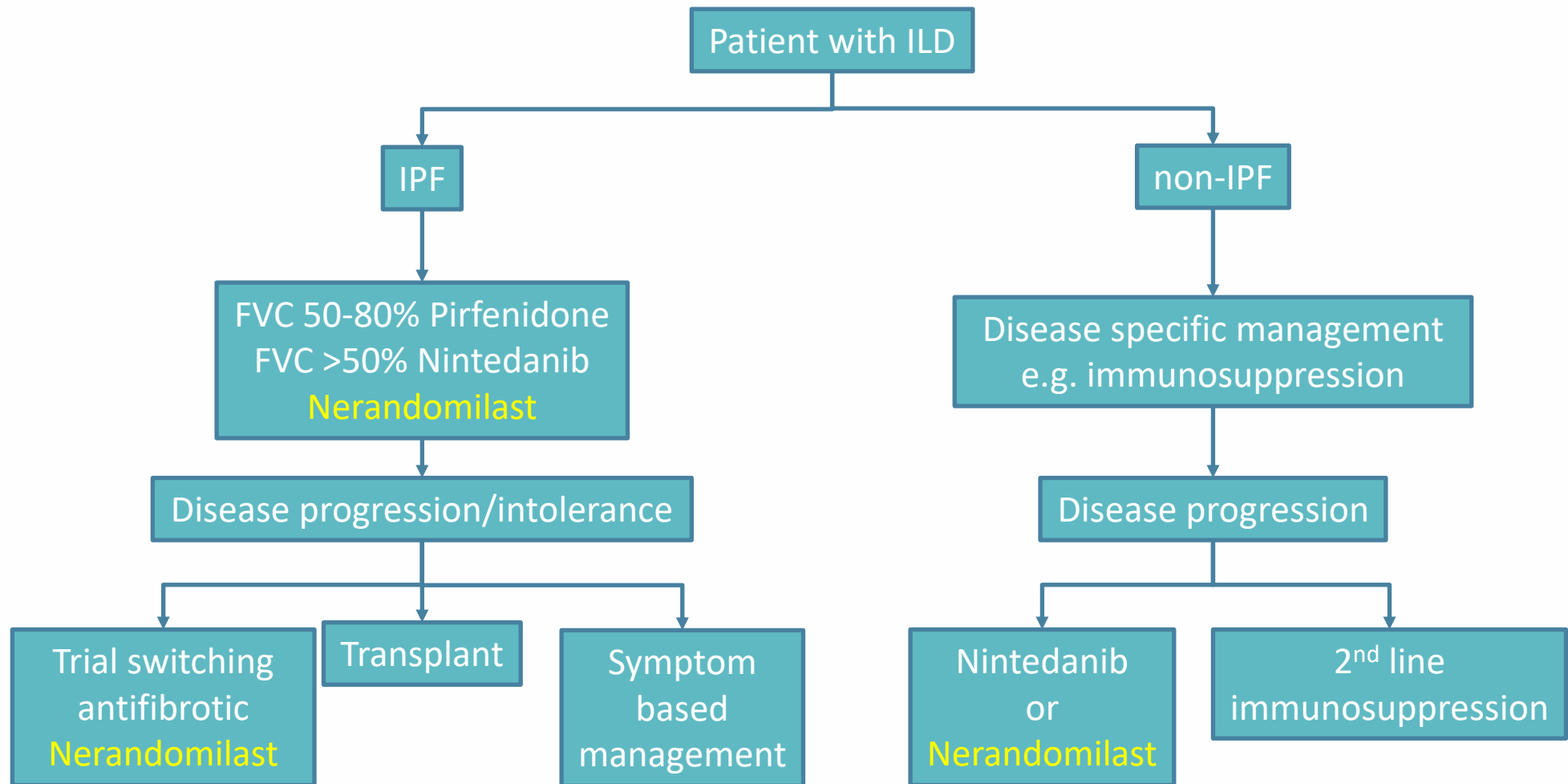
- July 2026 – MHRA approval for use in IPF and PPF in UK
- Ongoing NICE consultation
- Draft guidance available on NICE website
 - Current draft recommends “against use of Nerandomilast”
 - BUT expected publication date January 2027 for final guideline



How do we currently manage ILD in the UK?

Supportive and symptomatic care

- Pulmonary rehabilitation
- Palliative care
- Symptom management
- Psychological care
- Social care



Inhaled Treprostinil – TETON-1 and TETON-2



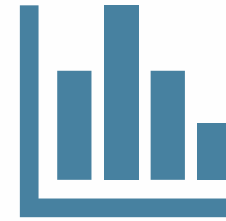
1191 patients
randomised across both
studies with IPF

- FVC >40%



Inhaled Treprostinil 12
breaths QDS vs placebo

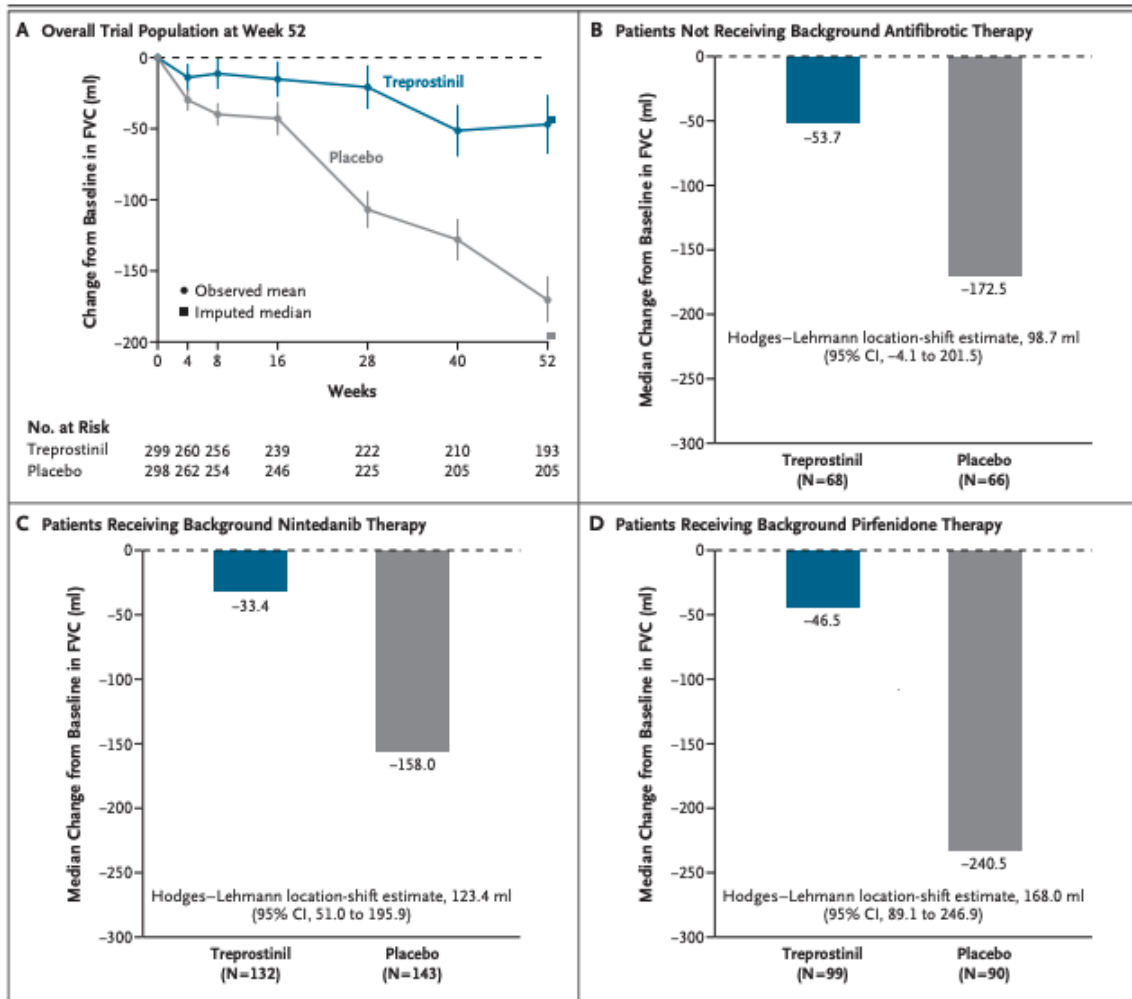
- Prostacyclin
analogue
- Prostacyclin
receptors modulate
fibrogenetic
pathways



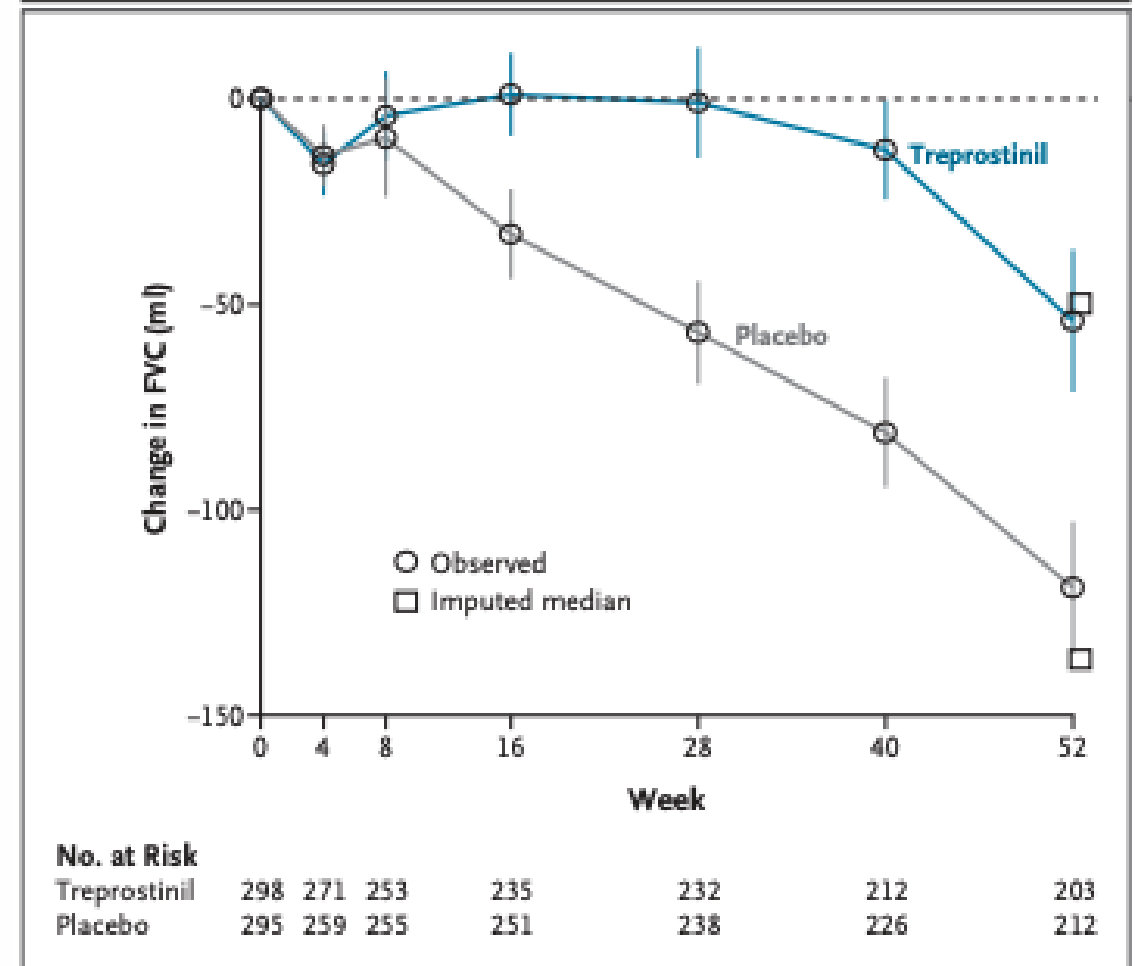
12 months
Randomised

- TETON-1 North
America
- TETON-2 Rest of
world

TETON 1



TETON 2



TETON 1 and 2 – Adverse events

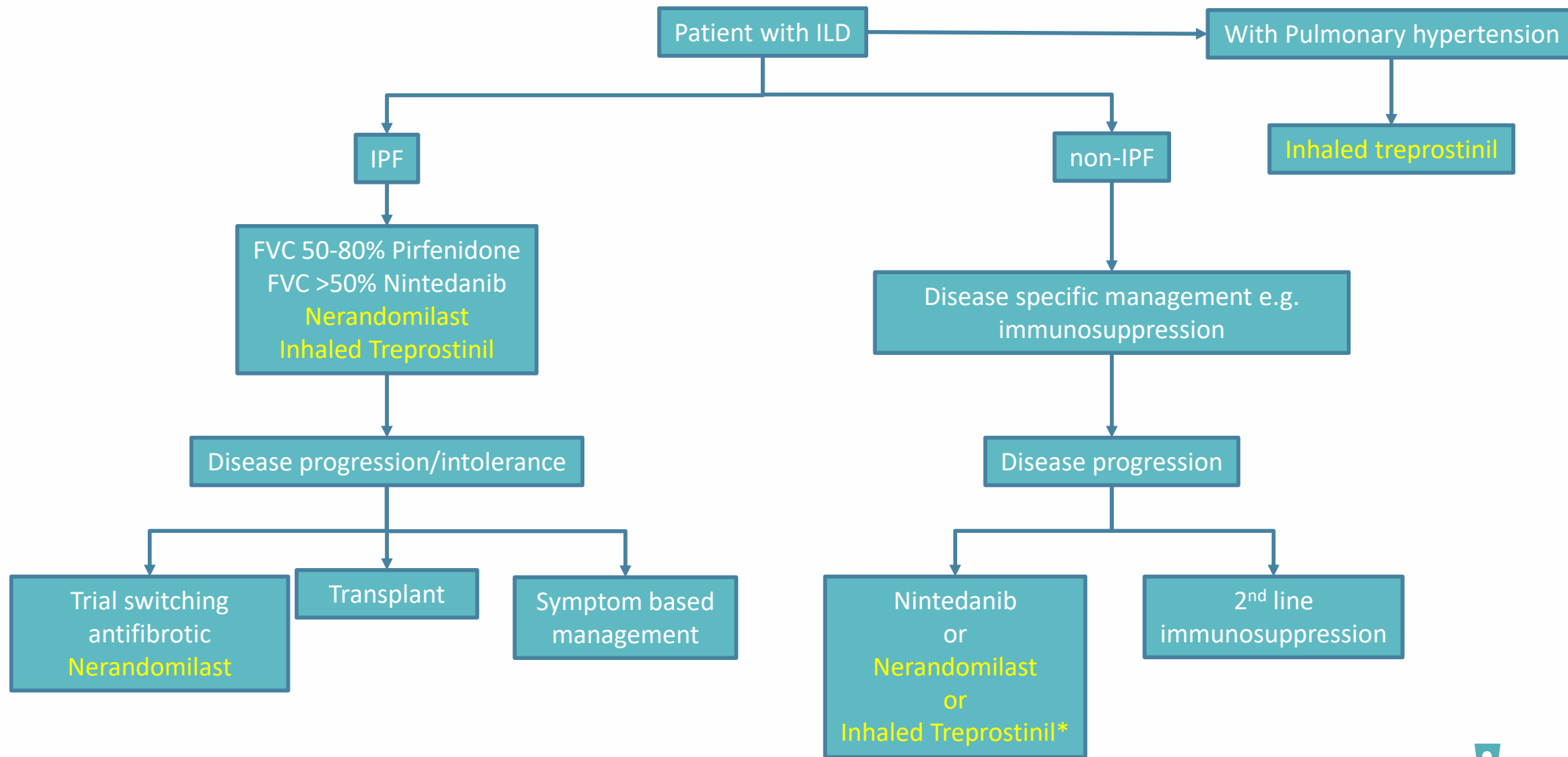
Adverse events	Treprostinil N=597, no. (%)	Placebo N=594, no. (%)
Cough	308 (51.6)	170 (28.6)
Headache	150 (25.1)	83 (14.0)
Dyspnoea	92 (15.4)	78 (13.1)
Diarrhoea	90 (15.1)	113 (19.0)
Dizziness	73 (12.2)	55 (9.3)
Fatigue	70 (11.7)	65 (10.9)
Throat irritation	63 (10.6)	23 (3.9)
Nausea	57 (9.5)	63 (10.6)
Nasopharyngitis	53 (8.9)	49 (8.2)



How do we currently manage ILD in the UK?

Supportive and symptomatic care

- Pulmonary rehabilitation
- Palliative care
- Symptom management
- Psychological care
- Social care

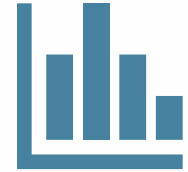


IPF and PPF Trials in development – new drug classes



ALOFT Study	IPF and PPF	Admilparent • LPA1 Antagonist	Phase 3 study has completed recruitment
ELEVATE-IPF	IPF	Deupirfenidone • Deuterated (chemically altered) version of pirfenidone possibly improved efficacy and tolerability	Phase 2b reported - positive Phase 3 protocol presented ERS 2026
MIST-PPF	PPF	Inhaled pirfenidone	Phase 2b study recruiting
WHISTLE PF	IPF	Taladegib • Hedgehog pathway inhibitor	Phase 2b study recruiting
AURORA	IPF	CAL101 (intravenous 4 weekly) • Antifibrotic and anti-inflammatory effect	Phase 2 study recruiting
RENEW Trial	IPF	LTI-03 • Inhaled calveolin-1 related peptide	Phase 2 study recruiting
WISPer	IPF	MTX-463 • WISP-1 inhibitor monoclonal antibody	Phase 2 study recruiting

IPF and PPF Trials in development

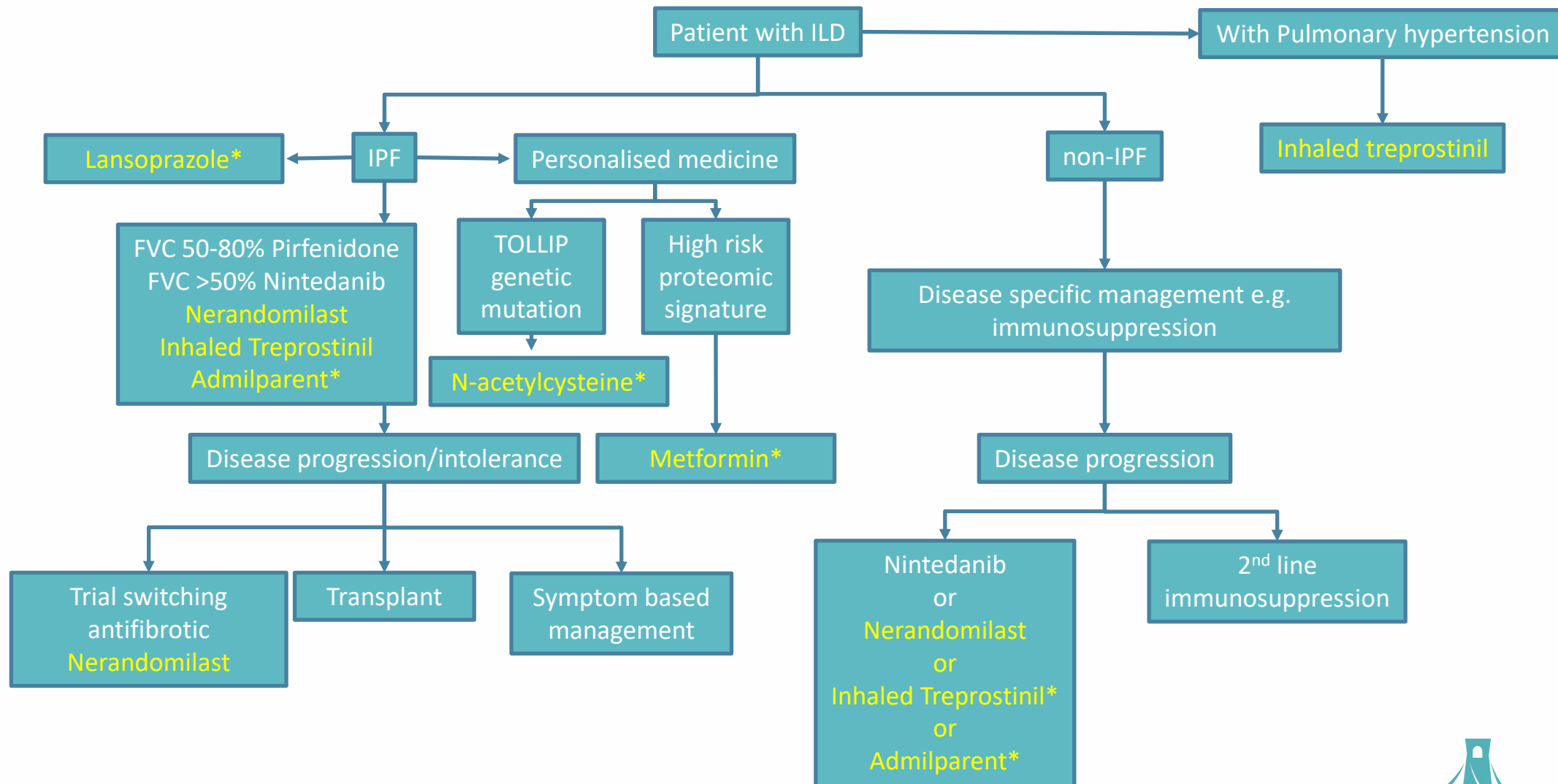


PRECISIONS-IPF	IPF with TOLLIP gene mutations (25% of IPF patients)	N-Acetylcysteine	Phase 3 completed recruitment and outcome awaited
TIPAL	IPF	Oral lansoprazole	Phase 3 study recruiting
MAVRIC	IPF with high risk of progression defined by proteomic signature	Oral Metformin	Phase 3 study recruiting

How do we currently manage ILD in the UK?

Supportive and symptomatic care

- Pulmonary rehabilitation
- Palliative care
- Symptom management
- Psychological care
- Social care



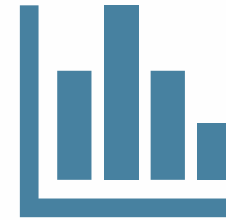
What about other ILD - CHORUS Study



Fibrotic hypersensitivity
pneumonitis



Oral Prednisolone vs
placebo



Currently recruiting
patients in the UK



What about other ILD – BEconneCTD-ILD Study



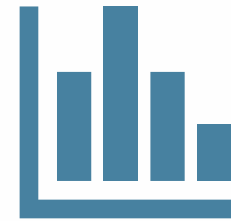
Connective tissue disease – ILD

- Excludes primary diagnosis of SSc



Belimumab

- Anti-Blys antibody
- Inhibits survival of B cells



Phase 3 study currently recruiting patients in the UK



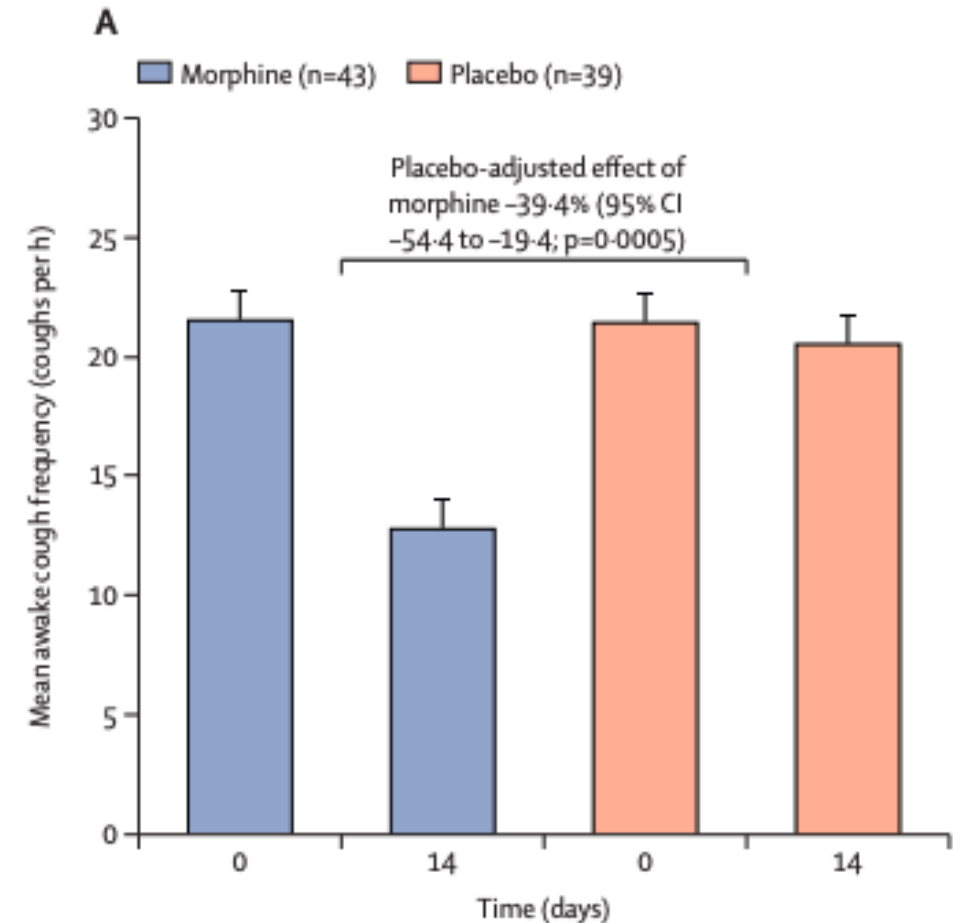
How can we improve symptoms?

Morphine for treatment of cough in idiopathic pulmonary fibrosis (PACIFY COUGH): a prospective, multicentre, randomised, double-blind, placebo-controlled, two-way crossover trial

Zhe Wu, Lisa G Spencer, Winston Banya, John Westoby, Veronica A Tudor, Pilar Rivera-Ortega, Nazia Chaudhuri, Ira Jakupovic, Brijesh Patel, Muhunthan Thillai, Alex West, Marlies Wijsenbeek, Toby M Maher, Jacky A Smith, Philip L Molyneaux



- Phase 2 study
- IPF and chronic cough
- Controlled release morphine 5mg BD vs placebo for 14 days then washout then crossover
- Outcome – Digital cough monitoring



Improving symptoms in ILD – CORAL study

JAMA | Original Investigation

Oral Nalbuphine in Idiopathic Pulmonary Fibrosis–Associated Cough The CORAL Randomized Clinical Trial

Philip L. Molyneux, MD, PhD; Nesrin Mogulkoc, MD; Hakan Gunen, MD; Anna Doboszyńska, MD;
Michael Kreuter, MD; Blue Neustifter, PhD; Vandana Mathur, MD; James Cassella, PhD;
for the CORAL Study Group

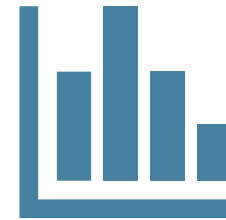


165 patients with IPF
with chronic cough



Oral nalbuphine
extended release

- κ opioid receptor agonist and μ -opioid receptor antagonist



Phase 2 b study

- 27mg BD
- 54mg BD
- 108mg BD
- Placebo BD

6 weeks

Relative change from baseline
in 24-hour cough frequency (coughs/h)



CORAL study - results

FINDINGS

Relative change in 24-hour cough frequency

	Coughs/hour at baseline	Coughs/hour at 6 weeks	Reduction in coughs/hour
Nalbuphine ER 27 mg	24.6 →	11.9	47.9%
Nalbuphine ER 54 mg	28.0 →	14.9	53.4%
Nalbuphine ER 108 mg	31.5 →	11.9	60.2%
Placebo	29.4 →	28.1	16.9%

The difficulty in improving symptoms

PFOX study (2026)	116 patients Fibrotic ILD with isolated exertional hypoxaemia <88% on 6MWT	Assigned 1:1 to ambulatory oxygen or sham oxygen device delivering air	No significant difference for change in mean steps per day at 3 months
MABEL study (2025)	MRC breathlessness score >3 due to cardiorespiratory conditions - 54 patients with ILD	5-10mg oral long-acting morphine or placebo	No significant effect on worst breathlessness score in the past 24 hours at day 28 Improved cough at day 56
BETTER-B study (2024)	COPD or ILD with MRC 3 or 4 - 101 ILD	Mirtazapine initially at 15mg and escalated to 45mg daily	No significant effect on worst breathlessness score in past 24 hours at 56 days • Increase in hospitalisation and informal caregiver hours



More positive news...

Specialist Dietary Intervention in Patients With Fibrotic Interstitial Lung Disease Experiencing Unintentional Weight Loss A Pilot Randomized Controlled Trial



Rasleen Kahai, BSc; Gioele Castelli, MD; Fiammetta Danzo, MD; Luis Ferreira, MD; Arthihai Srirangan, MD; Matteo Morviducci, MD; Flavio Marco Mirabelli, MD; Punchalee Kaenmuang, MD; Cara Roberts, MSc; Simon Bax, MD; Richard J. Hewitt, PhD; Maria Kokosi, MD; Felix Chua, PhD; Vasileios Kouranos, PhD; Philip L. Molyneaux, PhD; Peter M. George, PhD; Richard Gisli Jenkins, MD; Winston Banya, MSc; Carmel J. W. Stock, PhD; Steve Jones, BSc; Gemma Korff, BSc; Alastair Duncan, PhD; Athol U. Wells, MD; Piersante Sestini, MD; and Elisabetta A. Renzoni, PhD

- Pilot randomized controlled trial
- 40 patients with fibrotic-ILD and weightloss or low weight
- Randomised to
 - 12 week specialist dietary intervention
 - Dietary information sheet

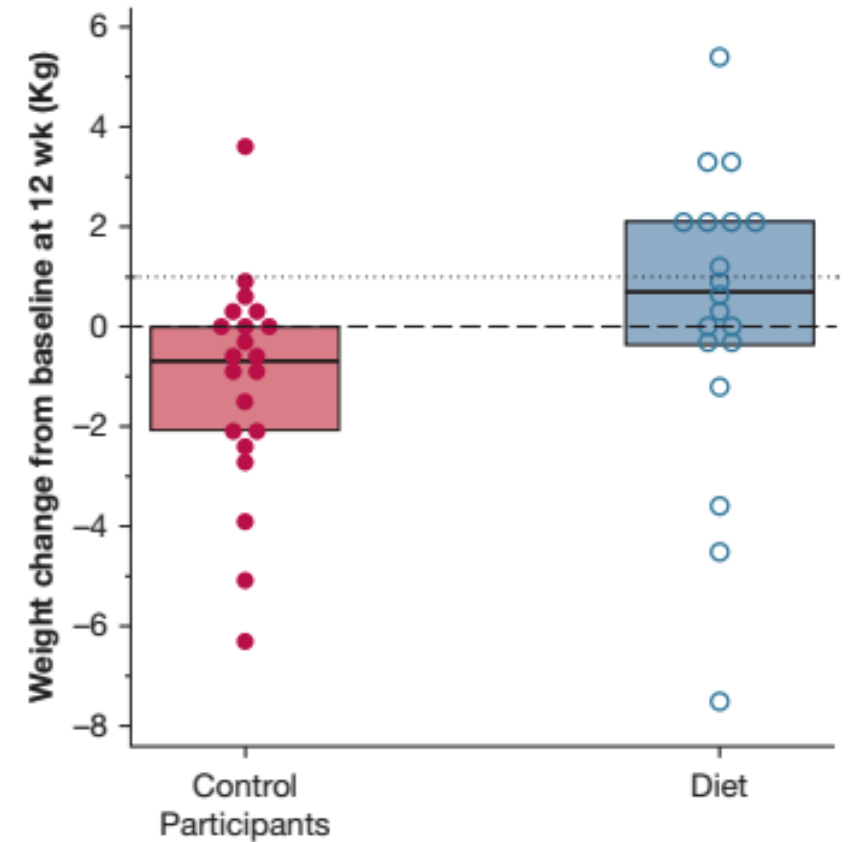


Figure 2 – Strip plot of weight changes at 12 weeks. Symbols represent individual patients in the control group (left, solid circles) and in the dietary intervention group (right, hollow circles). Superimposed box plots represent the median and interquartile range of each group. A horizontal dotted line is drawn to mark an increase of 1 kg.

More positive news...

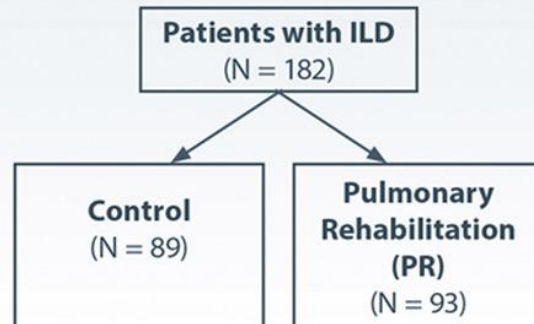
DIFFUSE LUNG DISEASE ■

Does Participation in Pulmonary Rehabilitation Impact Survival Among People With Interstitial Lung Disease?

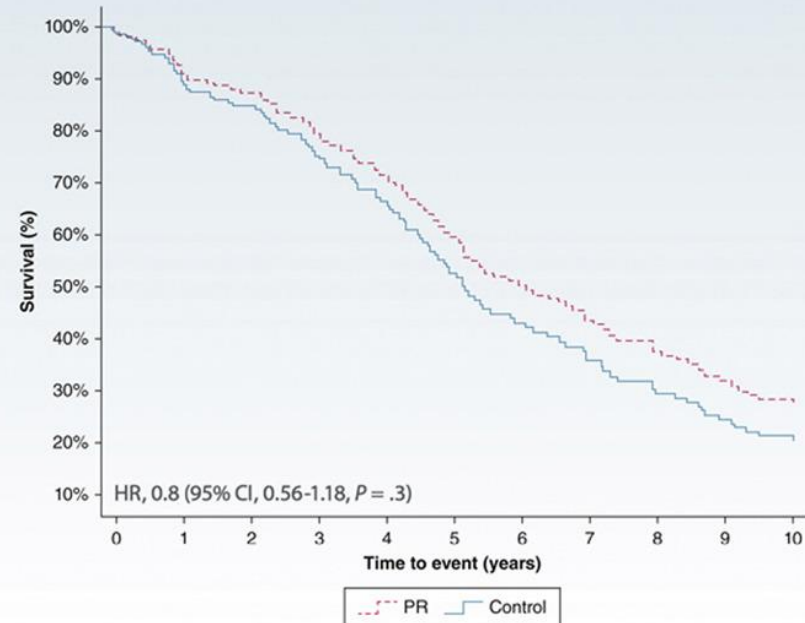


STUDY DESIGN

- Post hoc analysis of a combined cohort of two randomized controlled trials of patients with interstitial lung disease (ILD)
- **Primary End Point:** Death or lung transplantation



RESULTS



- After adjusting for baseline variables, at 5 years, completion of PR associated with a 44% lower risk of mortality (HR, 0.56; 95% CI, 0.36-0.88)
- At 10 years, no difference in survival was observed between the PR and control groups

Participation in PR among people with ILD may impact survival at 5 years.

Dowman LM, et al. *CHEST* June 2025 | @journal_CHEST | <https://doi:10.1016/j.chest.2025.01.001>

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Supportive care – Ongoing trials



Study Design: Multi-centre, wait-list design, randomised controlled trial

Disease Area: Respiratory

Funder: NIHR RfPB

Sponsor: Hull University Teaching Hospitals NHS Trust

Chief Investigator: Dr Ann Hutchinson

Trial registration: [ISRCTN13662540](https://www.isrctn.com/13662540)

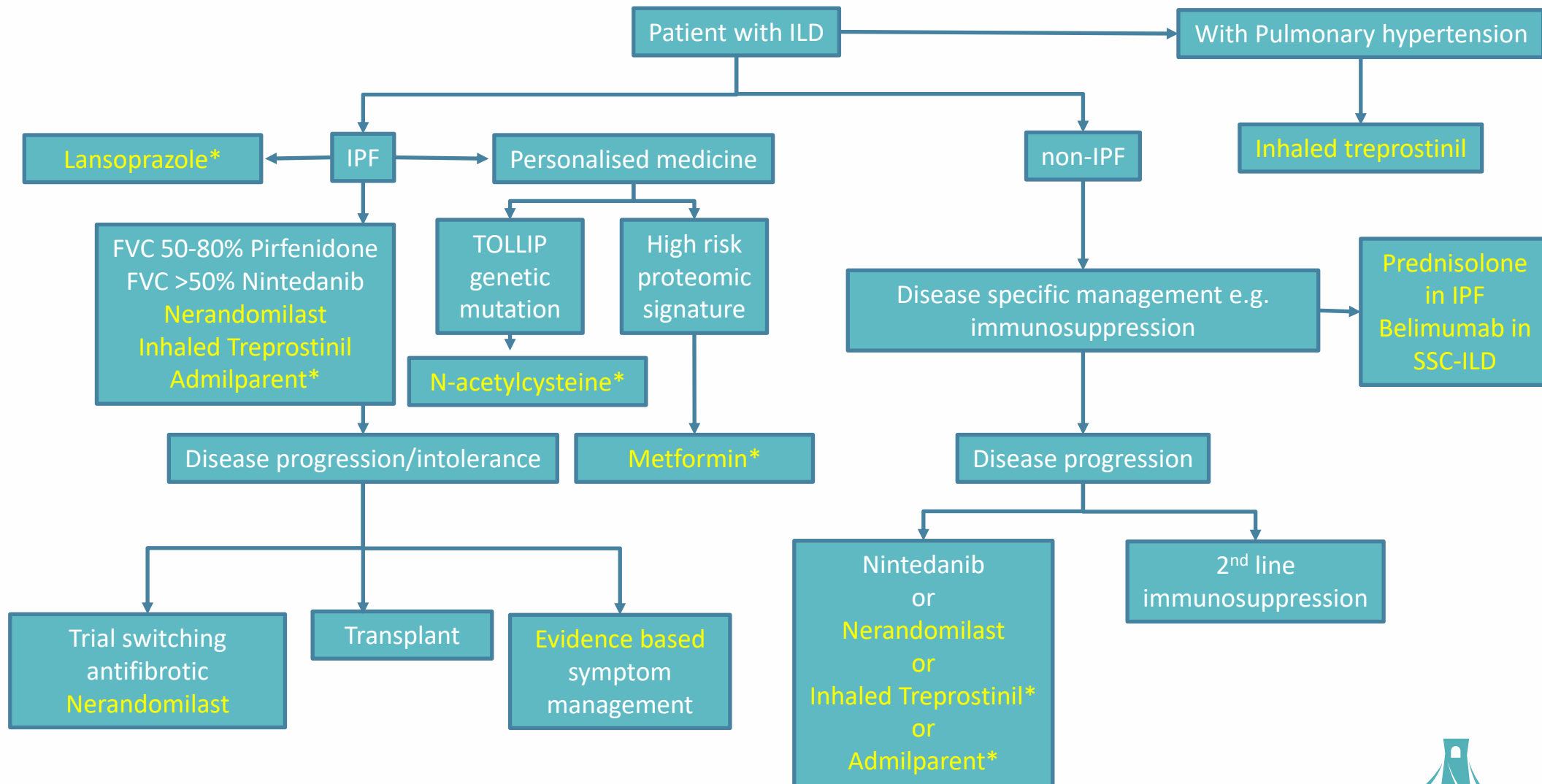
A randomised controlled trial of a complex intervention to manage breathlessness in pulmonary fibrosis (BREEZE-2)

- Currently recruiting
- Patients with pulmonary fibrosis and breathlessness
- Randomised to breathlessness management training at 1 week vs 8 weeks delivered by specialist nurses
- Outcome – Worst breathlessness in past 24 hours at 4 weeks

How do we currently manage ILD in the UK?

Evidence driven
supportive and
symptomatic care

- Pulmonary rehabilitation
- Palliative care
- Complex interventions
- Slow release morphine*/Na Ibuphine*
- Psychological care
- Social care
- Home monitoring
- Dietary intervention



But what have we missed?

How do we improve accuracy of diagnosis in PPF?

How do we know when to change treatment?

How can we reduce time taken to diagnosis?

How do we prognosticate in ILD?

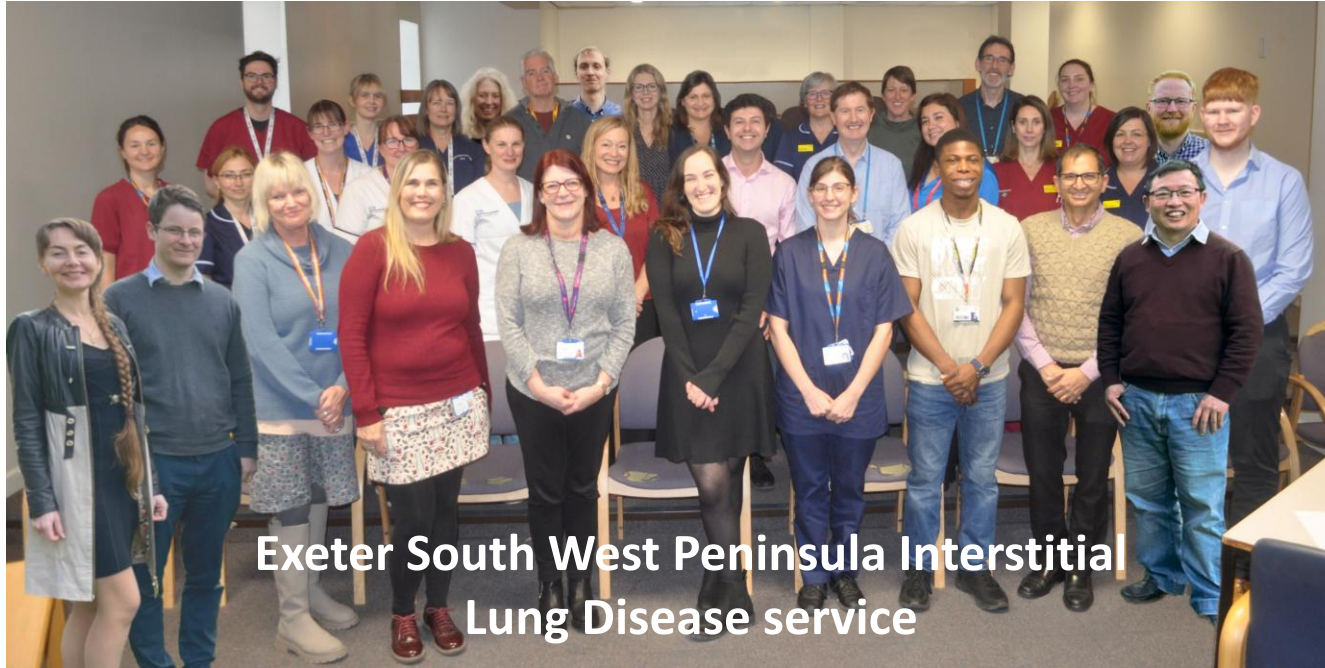
How can we improve end of life care in ILD?

How do we manage patients admitted to hospital with ILD?

How should we support caregivers?



Thank you



Exeter South West Peninsula Interstitial Lung Disease service

Royal Devon University Hospitals NHS Foundation Trust and Exeter South West Peninsula ILD service

- Pilar Rivera-Ortega
- Stefan Stanel
- Michael Gibbons

University of Exeter

Chris Scotton
Krasi Tsaneva-Atanasova



Bristol ILD Service

Bristol ILD Service

- Shaney Barratt
- Huzaifa Adamali
- Jo Hardy
- Matt Wells
- Sarah Mulholland
- Gabriella Ruffino

Royal United Hospitals Bath NHS Foundation Trust

- Tom Hartley
- Jonathan Rodrigues



A quick plug

- UK Interstitial Lung Disease Early Career Researcher Network
 - Meeting in Hull 21st and 22nd January 2027
 - All professions welcome
 - Friendly and welcoming meeting for those interested in a career in ILD research
 - dominic.sykes2@nhs.net



Any questions?

