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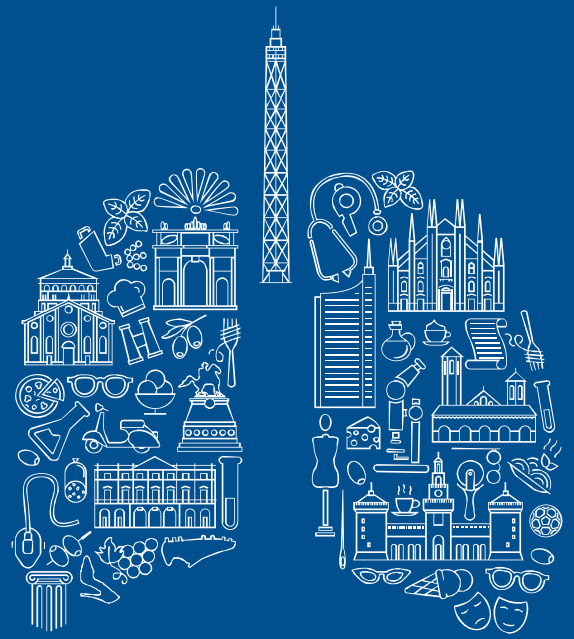

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Nebulised Pirfenidone in idiopathic pulmonary fibrosis (IPF): first look at FVC data

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Dr A Lawrence, H Bao, D Nair, C Thompson, Dr F Woodhead

11th September 2023

Conflict of interest disclosure

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I have the following real or perceived conflicts of interest that relate to this presentation:

Affiliation / Financial interest	Commercial company
Grants/research support:	
Honoraria or consultation fees:	Boehringer Ingelheim, (Avalyn Pharma Inc.)
Participation in a company sponsored bureau:	*Co-authors H Bao, D Nair, C Thompson & Dr F Woodhead are employees of Avalyn Pharma Inc*
Stock shareholder:	
Spouse / partner:	
Other support / potential conflict of interest:	

Content

1. Oral Pirfenidone: Side Effects
2. Nebulised Pirfenidone: Advantages
3. Study Structure
4. Efficacy: First look at FVC data
5. Comparing Side Effects

Oral Pirfenidone: Side Effects

Potentially dose and duration limiting

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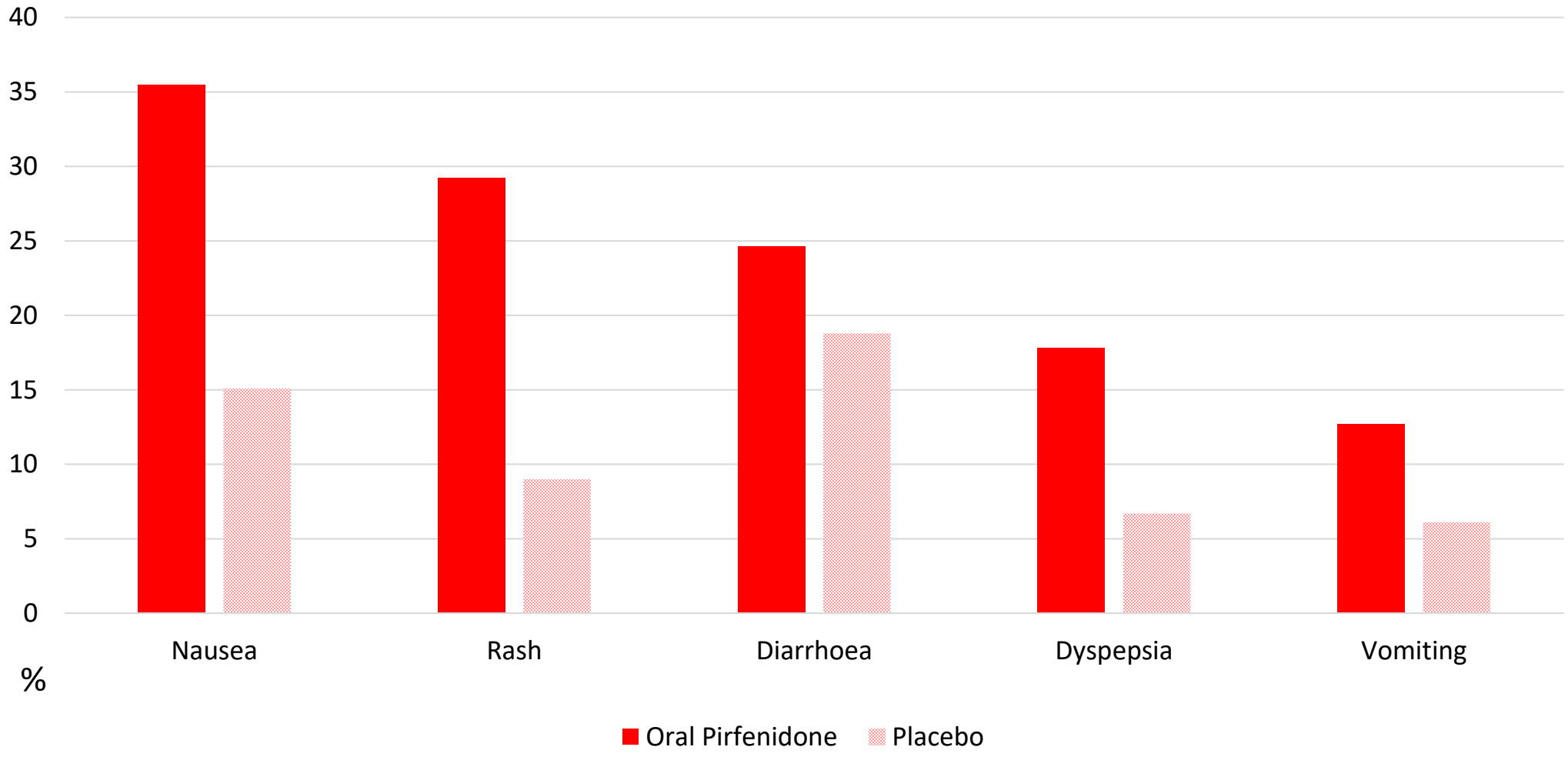

Noble, PW et al. Pirfenidone for idiopathic pulmonary fibrosis: analysis of pooled data from three multinational phase 3 trials, European Respiratory Journal 2016 47:243-253

Nebulised Pirfenidone: Advantages

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100 mg nebulised vs 801 mg oral

- x35 higher peak epithelial lining fluid concentration than oral
- <1/15th of the systemic exposure

Rubino, CM et al. Effect of food and antacids on the pharmacokinetics of pirfenidone in older healthy adults, Pulmonary Pharmacology & Therapeutics 2009, Aug;22(4):279-85
Kaminskas, LM et al. Aerosol Pirfenidone Pharmacokinetics after Inhaled Delivery in Sheep: a Viable Approach to Treating Idiopathic Pulmonary Fibrosis, Pharmaceutical Research 2020, 37:3

Study Structure
Open-Label Extension/Compassionate Use

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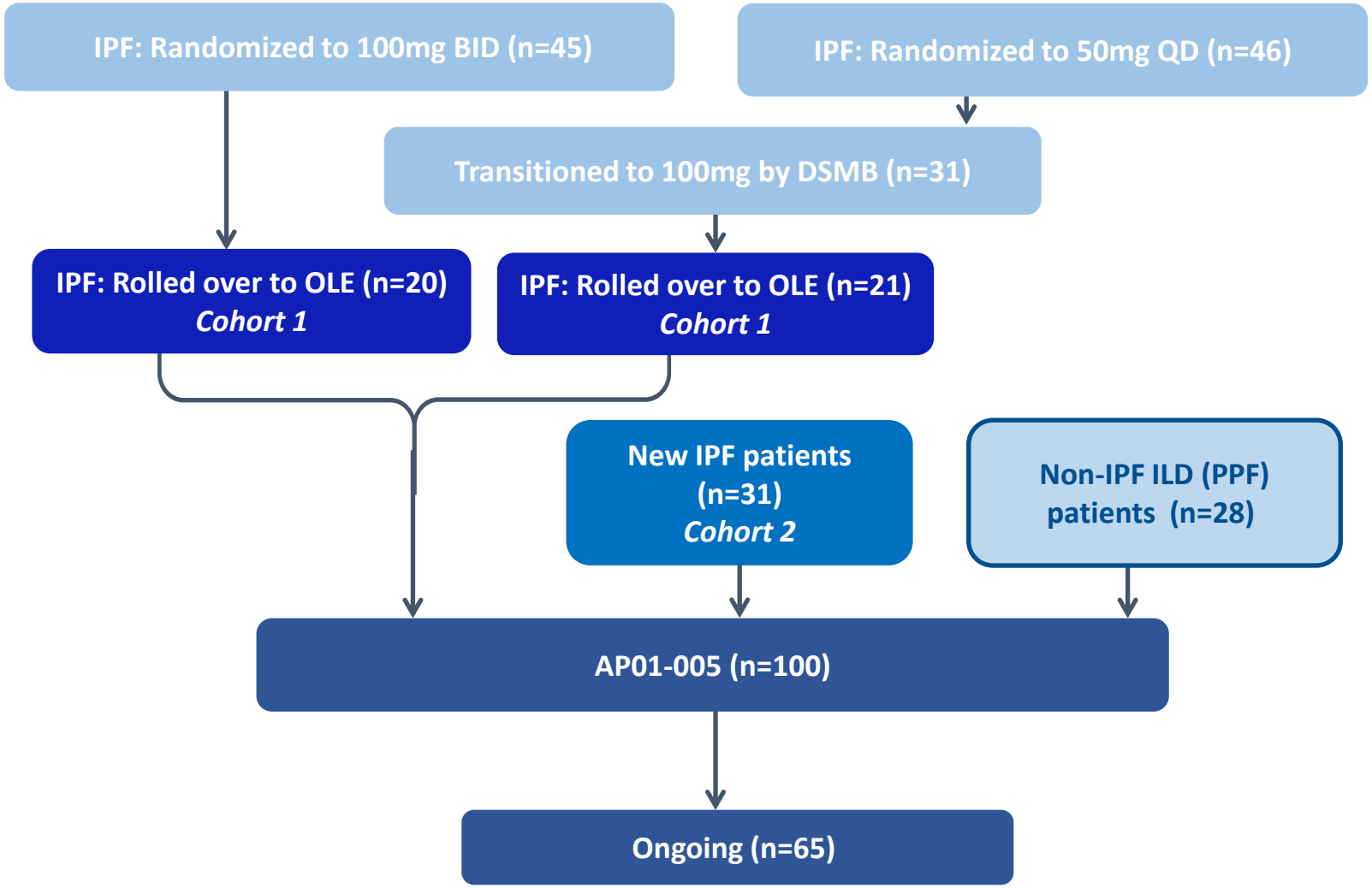
Interstitial lung disease

Original research

Inhaled pirfenidone solution (AP01) for IPF: a randomised, open-label, dose–response trial

Alex West,[1] Nazia Chaudhuri,[2] Adam Barczyk,[3] Margaret L Wilsher,[4] Peter Hopkins,[5] Ian Glaspole,[6] Tamera Jo Corte,[7,8] Martina Šterclová,[9] Antony Veale,[10] Ewa Jassem,[11] Marlies S Wijsenbeek,[12] Christopher Grainge,[13] Wojciech Piotrowski,[14] Ganesh Raghu,[15,16,17] Michele L Shaffer,[18] Deepthi Nair,[18] Lisa Freeman,[18] Kelly Otto,[18] A Bruce Montgomery[18]



n=41 from phase 1b (ATLAS)
n=31 newly recruited

Total IPF=72

Efficacy: First look at FVC data (48 weeks)

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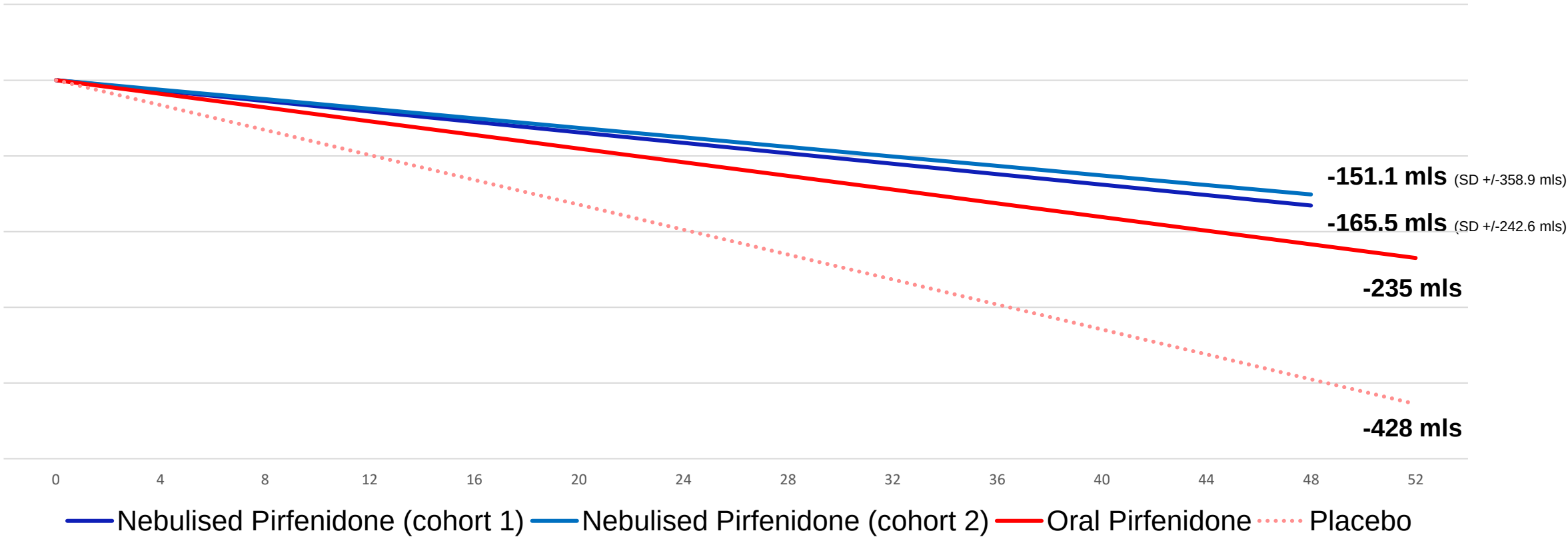
Change in FVC from Baseline



Talmadge Jr, EK et al. A Phase 3 Trial of Pirfenidone in Patients with Idiopathic Pulmonary Fibrosis, New England Journal of Medicine 2014; 370:2083-2092

Comparing Side Effects

Nebulised Pirfenidone vs Placebo vs Oral Pirfenidone

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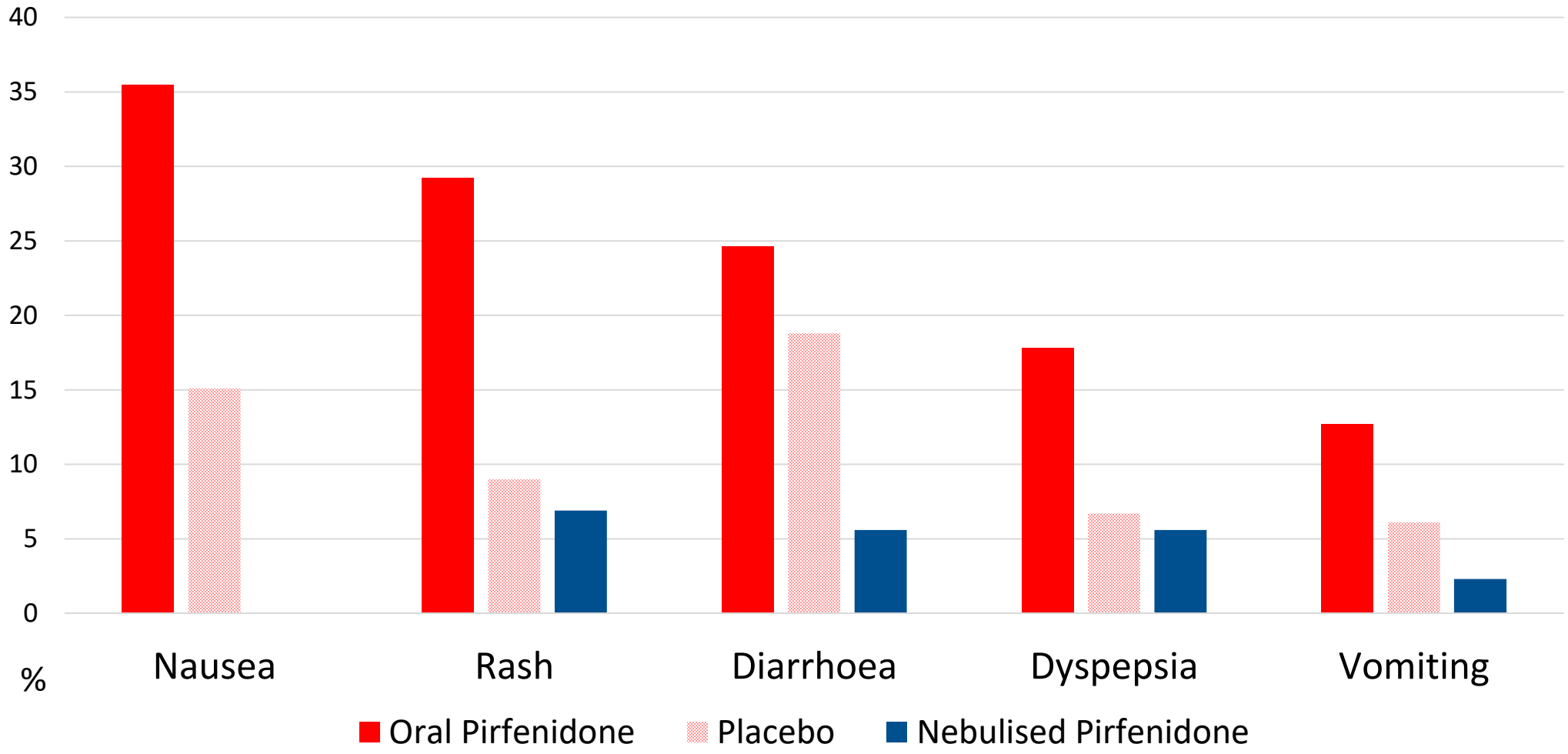

Noble, PW et al. Pirfenidone for idiopathic pulmonary fibrosis: analysis of pooled data from three multinational phase 3 trials, European Respiratory Journal 2016 47:243-253

Summary

Nebulised Pirfenidone vs Oral Pirfenidone

- x35 higher peak epithelial concentration than oral Pirfenidone
- <1/15th systemic absorption
- Early data suggests efficacy
- Less side effects

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All further contributors to the ATLAS study and ongoing open-label extension (AP01-005), including patients, investigators, and study teams from Australia, New Zealand, Czech Republic, The Netherlands, Poland and the UK, as well as the wider Avalyn Pharma Inc team.

Poster: Nebulised Pirfenidone for PPF

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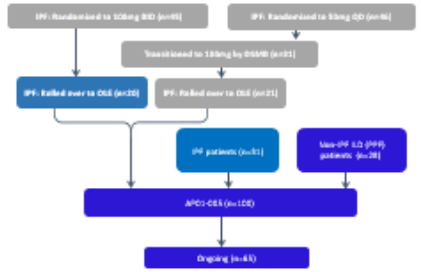
Nebulised pirfenidone in non-idiopathic pulmonary fibrosis (IPF) progressive pulmonary fibrosis (PPF): first look at FVC data

Dr A West[1], Dr A Lawrence[1], H Bao[2], D Nair[2], C Thompson[2], Dr F Woodhead[2]
[1]Guy's & St Thomas' NHS Foundation Trust- London (UK), [2]Avalyn Pharma Inc.- Seattle, Washington (USA)

Background

Oral antifibrotics attenuate the decline of lung function in patients with **progressive pulmonary fibrosis (PPF)** and oral Nintedanib is now considered standard of care. Side-effects, particularly gastrointestinal, are often reported with Nintedanib, and may lead to dose reduction or limitation of treatment.

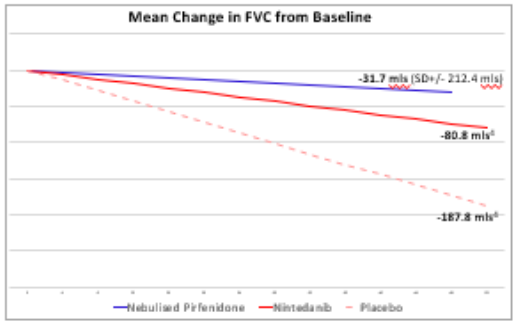
Nebulised Pirfenidone has been shown to be safe[1]. It has also been shown to achieve both **approximately x35 peak epithelial lining fluid concentration** (C_{max}) with **<1/15th systemic absorption**[2,3] of standard dose oral pirfenidone. This suggests the nebulised route has the potential both for effectiveness and improved tolerability.



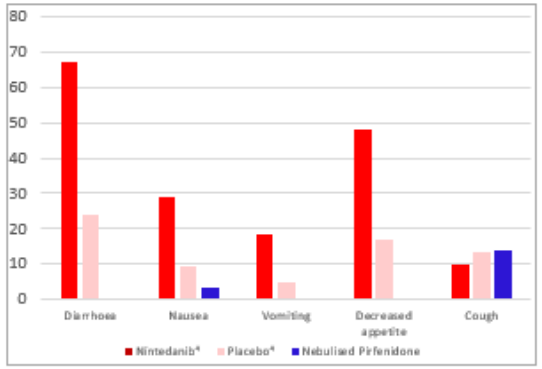
The **ATLAS** open-label extension was open to patients with **PPF**, and was designed to assess the safety of nebulised Pirfenidone. Patients were included if they had **chronic progressive fibrotic ILD** without treatment alternatives.

Baseline Characteristics & FVC Data

Baseline Characteristics	(n=28)
Age	63.8 yrs (SD+/-11.59)
Male : Female	12: 31
Baseline FVC	
<65%	39%
>65 to <80%	29%
>80%	32%
Mean FVC	75.3%p
Diagnoses	
CHP	14.3%
CTD-ILD	35.7%
Indeterminate IIP	42.9%
IPAF	3.6%
Pneumoconiosis	3.6%



Adverse Events



Nebulised Pirfenidone appears to be a **safe** and **well-tolerated** treatment in patients with **PPF**. **Cough** was the most commonly reported **adverse event (AE)** with a rate comparable to placebo. **Gastrointestinal** side-effects are markedly reduced compared with currently licensed treatment for **PPF**.

This first look at the **FVC data** suggests **nebulised Pirfenidone** is a promising development for the treatment of patients with **PPF**.

A Phase 2 study of **nebulised Pirfenidone** in **PPF** is planned and is aiming to recruit the first participant from early 2024.

Conflict of interest disclosure:
Dr A West: Honoraria from Boehringher Ingelheim, (Avalyn Pharma Inc.)
H Bao, D Nair, C Thompson, Dr F Woodhead: Employees of Avalyn Pharma Inc.

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4) Flaherty KR, et al. Nintedanib in Progressive Fibrosing Interstitial Lung Diseases. New England Journal of Medicine, 2019; 381:1718-1727

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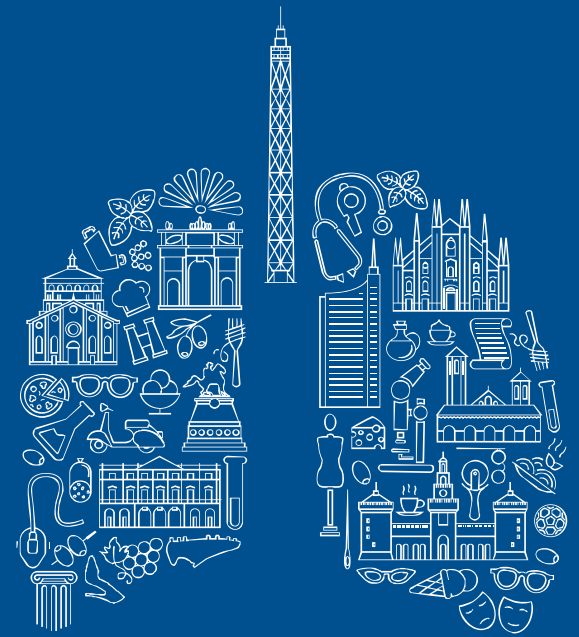

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