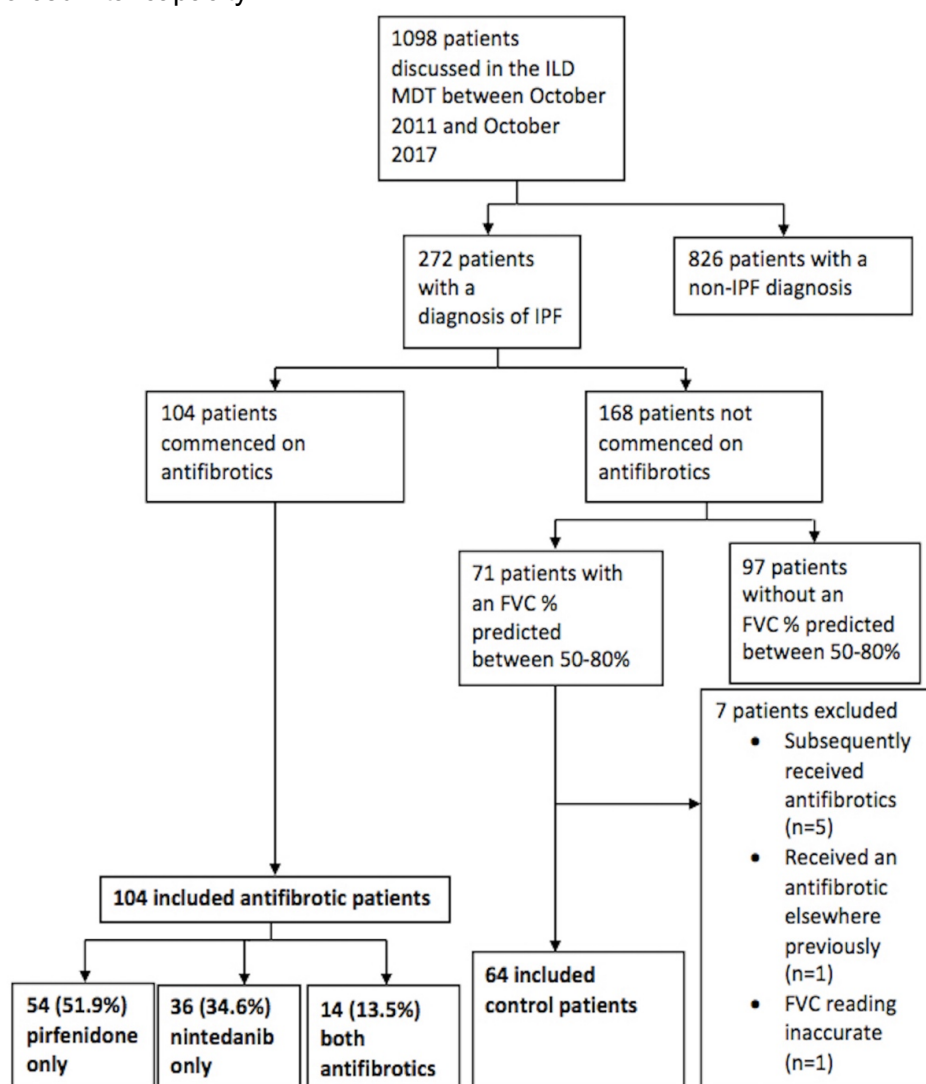


A real world retrospective observational study exploring the effectiveness and safety of antifibrotics in idiopathic pulmonary fibrosis
Wright WA et al.

Online Supplementary Material

Supplementary Figure 1: Consort diagram showing the process of patient inclusion and exclusion from analyses in the antifibrotic and control groups. 'Both antifibrotics' include patients who switched from one antifibrotic to another. ILD – interstitial lung disease, MDT – multi-disciplinary team, IPF – idiopathic pulmonary fibrosis, FVC – forced vital capacity.



Supplementary Table 1: Baseline characteristics of the patients who commenced pirfenidone first compared to those who commenced nintedanib first. IQR – interquartile range, BMI – body mass index, FVC - Forced vital capacity, DLco – diffusion capacity for carbon monoxide, Kco -carbon monoxide transfer coefficient, SpO₂ – pulse oximetry.

Characteristic		Pirfenidone (n=62)	Nintedanib (n=42)	P value
Male sex – no. (%)		45 (72.6)	34 (81.0)	0.327
Age – mean (SD)		69.9 (8.7)	72.6 (7.7)	0.108
Smoking status (%)				
	Never	19 (31.1)	14 (34.1)	
	Ex-smoker	40 (65.6)	27 (65.9)	
	Current smoker	2 (3.2)	0 (0.0)	
Smoking pack years (IQR)		17 (25)	8 (25)	0.381
Weight – Kg (SD)		81.8 (18.4)	77.3 (12.0)	0.197
BMI (IQR)		28.70 (6.27)	28.09 (4.70)	0.113
External referral (%)		35 (56.5)	22 (52.4)	0.682
Oxygen therapy (%)				
	LTOT	7 (11.3)	1 (2.4)	0.094
	Ambulatory	8 (12.9)	7 (16.7)	0.592
Previous triple therapy (%)		5 (8.1)	0 (0.0)	0.059
Previous corticosteroid therapy (%)		17 (27.4)	3 (7.1)	0.010
Histological diagnosis (%)		8 (12.9)	8 (19.0)	0.394
FVC – L (SD)		2.25 (0.50)	2.27 (0.53)	0.860
FVC % predicted (SD)		65.8 (9.3)	64.7 (8.5)	0.532
DLco – mmol/min/kPa (IQR)		3.21 (1.28)	3.48 (1.81)	0.215
DLco % predicted (SD)		41.5 (13.0)	45.2 (11.9)	0.167
Kco – mmol/min/kPa/L (SD)		1.04 (0.32)	1.13 (0.31)	0.219
Kco % predicted (SD)		77.5 (23.4)	84.7 (23.7)	0.153
SpO ₂ – % (IQR)		94 (5)	94 (4)	0.582
Emphysema on HRCT (%)		7	7	0.431

Supplementary Table 2: Effect of antifibrotic treatment on mortality at 6, 12 and 18 months with adjustment for independent predictors of mortality for each time point. Adjustment for baseline BMI ≤ 25 baseline and predicted DLco $\leq 35\%$ at 12 and 18 months. Adjustment for DLco $\leq 35\%$, Baseline eGFR ≤ 50 , Baseline neutrophil : lymphocyte ratio ≥ 5 at 6 months.

	Odds ratio (CI)	P Value
Antifibrotic treatment 6-month mortality	0.44 (0.14-1.31)	0.140
Antifibrotic treatment 12-month mortality	0.56 (0.24-1.30)	0.178
Antifibrotic treatment 18-month mortality	0.59 (0.27-1.32)	0.199

Univariate and multivariate analysis for 12-month mortality

Supplementary Table 3: Univariate analysis for 12-month mortality. Supplementary oxygen is patients on either LTOT or ambulatory oxygen therapy.

Variable	N	Odds ratio (CI)	Likelihood ratio	P value
Age ≥ 75	168	1.91 (0.97-3.74)	3.56	0.059
Male gender	168	1.32 (0.59-2.95)	0.45	0.507
Baseline BMI ≤ 25	166	3.69 (1.81-7.53)	13.12	<0.001
Baseline FVC % predicted $\leq 65\%$	167	1.39 (0.71-2.71)	0.90	0.342
Baseline DLco % predicted $\leq 35\%$	154	4.50 (2.11-9.59)	15.68	<0.001
Baseline oxygen saturations $\leq 94\%$	162	1.63 (0.81-3.28)	1.93	0.166
Baseline PPI treatment	168	0.95 (0.49-1.85)	0.02	0.876
Baseline statin treatment	168	1.23 (0.63-2.40)	0.36	0.551
Baseline supplementary oxygen	168	2.50 (1.09-5.76)	4.54	0.028
Prior steroid therapy	168	0.78 (0.29-2.11)	0.24	0.628
Baseline eGFR ≤ 50	167	1.47 (0.66-3.27)	0.87	0.344
Baseline neutrophil : lymphocyte ratio ≥ 5	166	1.94 (0.87-4.32)	2.52	0.104
Baseline platelet count ≤ 200	167	1.51 (0.75-3.04)	1.33	0.246

Supplementary Table 4: Multivariate analysis for 12-month mortality

Variable	Odds ratio (CI)	P value
Baseline BMI ≤ 25	3.30 (1.44-7.59)	0.005
Baseline DLco % predicted ≤ 35	3.30 (1.44-7.59)	0.005

Supplementary Table 5: Multivariate analysis for 6-month mortality

Variable	Odds ratio (CI)	P value
Baseline DLco % predicted ≤ 35	4.34 (1.47-13.12)	0.008
Baseline eGFR ≤ 50	4.51 (1.39-14.57)	0.012
Baseline neutrophil : lymphocyte ratio ≥ 5	3.63 (1.14-11.55)	0.029

Supplementary Table 6: Multivariate analysis for 18-month mortality

Variable	Odds ratio (CI)	P value
Baseline BMI ≤ 25	2.96 (1.33-6.57)	0.008
Baseline DLco % predicted ≤ 35	3.83 (1.73-8.51)	0.001

Supplementary Table 7: Multivariate analysis for 12-month mortality including only antifibrotic-treated patients

Variable	Odds ratio (CI)	P value
Baseline BMI ≤ 25	14.40 (3.68-56.34)	<0.001
Baseline platelet count ≤ 200	4.09 (1.13-14.77)	0.031
Discontinuation of an antifibrotic within 3 months	6.26 (1.54-25.52)	0.010

Univariate and multivariate analysis for PFS

Supplementary Table 8: Univariate analysis for 12-months PFS

Variable	N	Odds ratio (CI)	Likelihood ratio	P value
Age ≥ 75	168	0.48 (0.26-0.90)	5.32	0.022
Male gender	168	0.75 (0.37-1.54)	0.61	0.435
Baseline BMI ≤ 25	166	0.40 (0.20-0.79)	7.23	0.008
Baseline FVC % predicted $\leq 65\%$	167	1.41 (0.76-2.62)	1.17	0.279
Baseline DLco % predicted $\leq 35\%$	154	0.56 (0.28-1.11)	2.79	0.096
Baseline oxygen saturations $\leq 94\%$	162	0.71 (0.38-1.33)	1.16	0.283
Baseline PPI treatment	168	0.59 (0.32-1.10)	2.82	0.094
Baseline statin treatment	168	1.08 (0.59-1.99)	0.07	0.798
Baseline supplementary oxygen	168	0.44 (0.18-1.06)	3.64	0.061
Prior steroid therapy	168	1.91 (0.79-4.58)	2.11	0.145
Baseline eGFR ≤ 50	167	0.96 (0.45-2.05)	0.01	0.917
Baseline neutrophil : lymphocyte ratio ≥ 5	166	0.70 (0.32-1.54)	0.81	0.370
Baseline platelet count ≤ 200	167	0.83 (0.43-1.59)	0.32	0.573

Supplementary Table 9: Multivariate analysis for 12-month PFS

Variable	Odds ratio (CI)	P value
Age ≥ 75	2.12 (1.08-4.14)	0.029

Supplementary Table 10: 12-month PFS with antifibrotic treatment, adjusting for age >75

Variable	Odds ratio (CI)	P value
Age ≥ 75	1.79 (0.93-3.44)	0.081
Antifibrotic treatment	0.60 (0.31-1.18)	0.139

Multivariate analysis for 6-month PFS

No significant results.

Multivariate analysis for 18-month PFS

No significant results.

Antifibrotic discontinuation univariate and multivariate analysis

Supplementary Table 11: Univariate analysis for antifibrotic discontinuation by 12 months

Variable	N	Odds ratio (CI)	Likelihood ratio	P value
Age ≥75	104	2.35 (1.02-5.38)	4.13	0.042
Female sex	104	3.07 (1.20-7.82)	5.75	0.016
Baseline BMI ≤25	102	4.33 (1.66-11.28)	9.73	0.002
Baseline supplementary oxygen	104	1.80 (0.67-4.80)	1.38	0.239
Baseline DLco % predicted ≤35	96	2.07 (0.87-4.94)	2.74	0.097
Baseline FVC % predicted ≤65	103	0.75 (0.34-1.63)	0.54	0.463
Baseline oxygen saturations ≤94	101	1.50 (0.68-3.32)	1.01	0.316
Baseline eGFR ≤50	104	1.59 (0.59-4.31)	0.82	0.362
Baseline platelet count ≤200	104	1.78 (0.77-4.13)	1.82	0.176

Supplementary Table 12: Multivariate analysis for antifibrotic discontinuation by 12 months

Variable	Odds ratio (CI)	P value
Age ≥75	3.17 (1.16-8.68)	0.025
Female sex	4.57 (1.40-14.88)	0.012
Baseline BMI ≤25	3.74 (1.22-11.53)	0.021