

Supplementary Material

for

Disease Behaviour During the Peri-Diagnostic Period in Patients with Suspected

Interstitial Lung Disease: the STARLINER Study

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Fig. S1 Compliance with daily home spirometry measurements, including all blows, for (a) patients with IPF, and (b) patients with non-IPF ILD



b Patient ID number



ILD interstitial lung disease; *IPF* idiopathic pulmonary fibrosis

All blows are included in the figures. Measurements taken after treatment initiation have been removed from the analysis. Measurements collected more than 390 days after enrolment are not included

Table S1 Mandatory outcome measures

Home outcome measures
Daily FVC assessed using home spirometry
Daily physical functional capacity (steps per day) assessed using a smartwatch accelerometer
Site outcome measures
FVC assessed using site spirometry at mandatory site visits and any additional visits scheduled at the clinician's discretion
6MWD assessed at mandatory site visits and any additional visits scheduled at the clinician's discretion
Patient-reported outcomes
K-BILD
EQ-5D-5L
FAS
Fatigue VAS
Cough VAS
Urge-to-cough VAS
mMRC

6MWD 6-minute walk distance; *EQ-5D-5L* EuroQoL 5 Dimensions 5-level index questionnaire; *FAS* Fatigue Assessment Scale; *FVC* forced vital capacity; *K-BILD* King's Brief Interstitial Lung Disease questionnaire; *mMRC* modified Medical Research Council; *VAS* visual analogue scale

Table S2 Quality criteria for home FVC measurements

Acceptable manoeuvre	Unacceptable manoeuvre
• Don't start too early • Avoid coughing • Good blow	• Blow out faster • Blow out longer • Abrupt end

FVC forced vital capacity

Table S3 Non-IPF ILD diagnoses

Type of ILD <i>n</i> (%)	Non-IPF ILD <i>N</i> = 62
ILD of known causes	
CTD	5 (8.1)
Autoimmune disease	1 (20.0)
Rheumatoid arthritis	2 (40.0)
Systemic sclerosis/scleroderma	1 (20.0)
Unspecified CTD	1 (20.0)
Vascular disease	1 (1.6)
Systemic lupus erythematosus	1 (100)
Exposures	2 (3.2)
Asbestos	2 (100)
Drugs	1 (1.6)
Teriflunomide	1 (100)
Idiopathic non-specific interstitial pneumonia	13 (21.0)
Desquamative interstitial pneumonia	1 (1.6)
Cryptogenic organising pneumonia	3 (4.8)
Acute interstitial pneumonia	1 (1.6)
Lymphocytic interstitial pneumonia	1 (1.6)
Unclassifiable ILD	13 (21.0)
Hypersensitivity pneumonitis	10 (16.1)
Sarcoidosis	5 (8.1)
Eosinophilic pneumonia	1 (1.6)
Other ^a	5 (8.1)

CTD connective tissue disease; *ILD* interstitial lung disease; *IPF* idiopathic pulmonary fibrosis

^a The following specifications were provided for patients in the 'Other' category: combined pulmonary fibrosis and emphysema, *n* = 2; reticulonodular interstitial disease secondary to smoke-related interstitial fibrosis, *n* = 1; mild ILD of unknown aetiology, *n* = 1; interstitial pneumonia with autoimmune features, *n* = 1

Table S4 Assessments used for diagnosis

	IPF N = 68	Non-IPF ILD N = 62
HRCT	67 (98.5)	57 (91.9)
BAL	31 (45.6)	21 (33.9)
Lung biopsy	17 (25.0)	14 (22.6)
Surgical lung biopsy	8 (11.8)	7 (11.3)
Transbronchial cryobiopsy	7 (10.3)	7 (11.3)
Other ^a	2 (2.9)	0

BAL bronchoalveolar lavage; *HRCT* high-resolution computed tomography; *ILD* interstitial lung disease; *IPF* idiopathic pulmonary fibrosis

^a No further specification was available

Table S5 Patient disposition and treatment initiation

Patient disposition	IPF N = 68	Non-IPF ILD N = 62
Number of patients enrolled in the study	68 (100)	62 (100)
Number of patients who discontinued from the study prematurely		
At the end of the pre-diagnostic period	3 (4.4)	17 (27.4)
At the end of the post-diagnostic period	1 (1.5)	4 (6.5)
Number of patients who completed the study		
At the end of the pre-diagnostic period	29 (42.6)	21 (33.9)
At the end of the post-diagnostic period	35 (51.5)	20 (32.3)
Number of patients who completed the study without the start of treatment	5 (7.4)	15 (24.2)
Number of patients who completed the study with the start of treatment	59 (86.8)	26 (41.9)
Treatment		
Pirfenidone	34 (50.0)	0 (0.0)
Nintedanib	25 (36.8)	1 (1.6)
NAC	0 (0.0)	1 (1.6)
Corticoid treatment	0 (0.0)	18 (29.0)
Cyclophosphamide	0 (0.0)	0 (0.0)
Azathioprine	0 (0.0)	0 (0.0)
Mycophenolate mofetil	0 (0.0)	3 (4.8)
Methotrexate	0 (0.0)	0 (0.0)
Cyclosporine	0 (0.0)	0 (0.0)
Other	0 (0.0)	3 (4.8)

IPF idiopathic pulmonary fibrosis; *NAC* N-acetylcysteine

Table S6 Summary of semi-annual change in lung function and exercise capacity during the peri-diagnostic period estimated from a linear regression model^a in patients with IPF and non-IPF ILD

	IPF N = 68		Non-IPF ILD N = 62	
	All patients	Sensitivity analysis excluding patients with <30 days' observation time	All patients	Sensitivity analysis excluding patients with <30 days' observation time
Semi-annual FVC change including only 'good blows', measured using home spirometry, mL				
Observed, <i>n</i>	64	51	59	52
Mean (95% CI)	-308.7 (-625.6, 8.2)	-219.4 (-572.0, 133.3)	57.5 (-275.3, 390.3)	35.8 (-174.3, 245.8)
Semi-annual FVC change including all 'acceptable blows', measured using home spirometry, mL				
Observed, <i>n</i>	65	53	60	52
Mean (95% CI)	-535.7 (-1193.3, 127.8)	-48.8 (-511.3, 413.6)	279.5 (-239.4, 798.3)	198.0 (-31.5, 427.5)
Semi-annual FVC change measured using site spirometry, mL				
Observed, <i>n</i>	63	57	60	56
Mean (95% CI)	-154.1 (-286.6, -21.6)	-130.1 (-257.6, -2.6)	-209.0 (-700.1, 282.1)	15.7 (-67.2, 98.6)
Semi-annual 6MWD change measured at site visits, m				
Observed, <i>n</i>	59	53	55	51
Mean (95% CI)	29.2 (-35.4, 93.7)	13.9 (-38.7, 66.6)	195.5 (-192.5, 583.4)	-3.5 (-32.4, 25.4)
Semi-annual change in functional capacity measured using daily accelerometry, steps per day				
Observed, <i>n</i>	66	53	61	53
Mean (95% CI)	-1237.2 (-4714.7, 2240.3)	-1119.1 (-3417.4, 1179.1)	-13 407.3 (-32,004.3, 5189.7)	-1432.8 (-2874.6, 9.0)

6MWD 6-minute walk distance; CI confidence interval; FVC forced vital capacity; ILD interstitial lung disease; IPF idiopathic pulmonary fibrosis

^a Only patients with at least three measurements are included in the linear regression model

Table S7 Shift table of mMRC scores in patients with IPF and non-IPF ILD

		Score at baseline					Missing	Total
		0	1	2	3	4		
Patients with IPF, <i>n</i> (%)								
Score at end of study visit	0	10 (14.7)	6 (8.8)	0	1 (1.5)	0	0	17 (25.0)
	1	7 (10.3)	18 (26.5)	6 (8.8)	0	0	0	31 (45.6)
	2	1 (1.5)	5 (7.4)	3 (4.4)	1 (1.5)	0	0	10 (14.7)
	3	1 (1.5)	0	1 (1.5)	3 (4.4)	0	0	5 (7.4)
	4	0	0	0	0	0	0	0
	Missing	1 (1.5)	1 (1.5)	0	0	0	0	2 (2.9)
Total		20 (29.4)	30 (44.1)	10 (14.7)	5 (7.4)	0	0	65 (95.6)
Patients with non-IPF ILD, <i>n</i> (%)								
Score at end of study visit	0	12 (19.4)	3 (4.8)	3 (4.8)	0	0	1 (1.6)	19 (30.6)
	1	3 (4.8)	13 (21.0)	2 (3.2)	1 (1.6)	0	0	19 (30.6)
	2	0	5 (8.1)	9 (14.5)	1 (1.6)	0	0	15 (24.2)
	3	1 (1.6)	1 (1.6)	2 (3.2)	1 (1.6)	0	0	5 (8.1)
	4	0	1 (1.6)	0	0	0	0	1 (1.6)
	Missing	1 (1.6)	2 (3.2)	0	0	0	0	3 (4.8)
Total		17 (27.4)	25 (40.3)	16 (25.8)	3 (4.5)	0	1 (1.6)	62 (100)

ILD interstitial lung disease; *IPF* idiopathic pulmonary fibrosis; *mMRC* modified Medical Research Council dyspnoea scale
For mMRC scores, a higher score indicates greater dyspnoea

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Site number	Investigator	Name and Address of Ethics Committee/Institutional Review Board	Date of Approval
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303174	M. Smirnov	Vladimir Region "Regional Clinical Hospital" Ethics Committee, 41, Sudogodskoye Shosse, Vladimir, Russia	25-Aug-2017
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303188	N. Revel-Muroz	Chelyabinsk Regional Clinical Hospital Ethics Committee, 70, Vorovskogo str., Chelyabinsk, Russia	06-Oct-2017
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