Progressive fibrosing interstitial lung disease: a clinical cohort (the PROGRESS® study)

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Online supplement

Supplementary Table S1. Medical history of the patient cohort

	Patients (N=165)
Respiratory medical conditions, n (%)	
Asthma	4 (2.4)
Emphysema	9 (5.5)
Ischaemic heart disease	14 (8.5)
Acute respiratory distress syndrome	1 (0.6)
Pulmonary hypertension (transthoracic cardiac ultrasound)	12 (7.3)
Other medical conditions, n (%)	
Hypertension	49 (29.7)
Gastroesophageal reflux disease	26 (15.8)
Raynaud phenomenon	46 (27.9)
Dysthyroidism	13 (7.9)
Diabetes mellitus	34 (20.6)

Supplementary Table S2. Autoantibodies detected in patient cohort

Autoantibodies	N documented	Patients, n (%)
Anti-centromere	148	4 (2.7)
Anti-SSA/Ro	157	9 (5.7)
Anti-Scl-70 (anti-topoisomerase-1)	152	24 (15.8)
Anti-Jo-1	156	10 (6.4)
Anti-PM/Scl-75	41	3 (7.3)
Rheumatoid factor	149	29 (19.5)
ANCA	106	18 (17.0)
c-ANCA	109	4 (3.7)
p-ANCA	109	2 (1.8)

ANCA, antineutrophil cytoplasmic antibodies; c-ANCA, cytoplasmic antineutrophil cytoplasmic antibodies; p-ANCA, perinuclear antineutrophil cytoplasmic antibodies; PM/Scl-75, exosome; SSA, Sjögren's-syndrome-related antigen A.

Supplementary Table S3. Overall survival according to FVC at inclusion with a 70% threshold

	Progressive fibrosing ILD (n=165)	
	FVC <70% at inclusion (n=56)	**FVC ≥70% at inclusion (n=82)**
OS rate, % (95% CI)		
12 months	98.0 (86.6–99.7)	98.7 (90.9–99.8)
24 months	89.6 (76.8–95.5)	90.1 (80.3–95.1)
36 months	77.1 (61.4–87.1)	83.4 (71.9–90.5)
48 months	68.2 (51.2–80.4)	77.0 (63.9–85.9)
60 months	64.4 (46.7–77.6)	69.5 (54.7–80.2)
72 months	52.4 (33.6–68.1)	69.5 (54.7–80.2)
84 months	52.4 (33.6–68.1)	69.5 (54.7–80.2)

Overall survival was defined as the time in months from date of disease progression to the date of death due to any cause or the end of follow-up.

CI, confidence interval; FVC, forced vital capacity; ILD, interstitial lung disease; OS, overall survival.

Supplementary Table S4. Overall survival according to GAP index

	Progressive fibrosing ILD (n=165)	
	GAP index Stage I (n=81)	**GAP index Stage II/III (n=45)**
OS rate, % (95% CI)		
12 months	98.7 (91.1–99.8)	97.3 (82.3–99.6)
24 months	90.5 (81.1–95.4)	88.5 (72.2–95.5)
36 months	87.4 (77.2–93.3)	71.3 (51.7–84.1)
48 months	81.6 (69.6–89.2)	62.4 (41.6–77.5)
60 months	72.8 (58.9–82.7)	56.1 (34.2–73.3)
72 months	66.9 (51.5–78.4)	56.1 (34.2–73.3)
84 months	66.9 (51.5–78.4)	56.1 (34.2–73.3)

Overall survival was defined as the time in months from date of disease progression to the date of death due to any cause or the end of follow-up.

CI, confidence interval; GAP, Gender, Age and Physiology; ILD, interstitial lung disease; OS, overall survival.

Supplementary Table S5. Overall survival according to disease subgroups

	Progressive fibrosing ILD (n=165)		
	Unclassifiable ILD + IIP + HP (n=78)	**Autoimmune ILD (n=77)**	**Other ILD + sarcoidosis (n=10)**
OS rate, % (95% CI)			
12 months	98.6 (90.4–99.8)	98.6 (90.2–99.8)	87.5 (38.7–98.1)
24 months	88.2 (77.8–93.9)	93.9 (84.5–97.7)	87.5 (38.7–98.1)
36 months	71.0 (57.8–80.8)	92.2 (82.2–96.7)	87.5 (38.7–98.1)
48 months	64.6 (50.7–75.6)	88.1 (76.4–94.2)	87.5 (38.7–98.1)
60 months	52.3 (37.5–65.2)	85.5 (72.6–92.6)	65.6 (15.7–90.9)
72 months	49.1 (33.9–62.5)	80.2 (65.5–89.1)	65.6 (15.7–90.9)
84 months	49.1 (33.9–62.5)	80.2 (65.5–89.1)	65.6 (15.7–90.9)

Overall survival was defined as the time in months from date of disease progression to the date of death due to any cause or the end of follow-up.

CI, confidence interval; HP, hypersensitivity pneumonitis; IIP, idiopathic interstitial pneumonia; ILD, interstitial lung disease; OS, overall survival.

Supplementary Table S6. Overall survival according to criteria for progression

	Progressive fibrosing ILD (n=165)		
	Relative FVC decline ≥10% at baseline (n=109)	**Relative decline of 5–<10% of predicted value plus worsening of respiratory symptoms or increased extent of fibrosis on HRCT (n=41)**	**Worsening of respiratory symptoms and increased extent of fibrosis with a relative FVC decline of <5% (n=15)**
OS rate, % (95% CI)			
12 months	99.0 (93.0–99.9)	97.0 (80.4–99.6)	91.7 (53.9–98.8)
24 months	87.1 (78.4–92.5)	97.0 (80.4–99.6)	91.7 (53.9–98.8)
36 months	79.9 (69.9–86.8)	87.3 (69.5–95.0)	91.7 (53.9–98.8)
48 months	74.2 (63.3–82.3)	76.9 (57.5–88.3)	91.7 (53.9–98.8)
60 months	70.8 (59.4–79.6)	69.0 (48.4–82.6)	91.7 (53.9–98.8)
72 months	60.9 (47.9–71.5)	69.0 (48.4–82.6)	91.7 (53.9–98.8)
84 months	60.9 (47.9–71.5)	69.0 (48.4–82.6)	91.7 (53.9–98.8)

Overall survival was defined as the time in months from date of disease progression to the date of death due to any cause or the end of follow-up.

CI, confidence interval; FVC, forced vital capacity; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; OS, overall survival.

Supplementary Table S7. Overall survival according to UIP-like pattern on HRCT at baseline

	Progressive fibrosing ILD (n=165)	
	UIP-like (n=46)	**Non-UIP-like (n=119)**
OS rate, % (95% CI)		
12 months	97.6 (84.3–99.7)	99.1 (93.6–99.9)
24 months	87.3 (72.0–94.5)	92.3 (85.1–96.1)
36 months	81.1 (64.1–90.6)	83.6 (74.5–89.6)
48 months	77.2 (59.0–88.1)	75.9 (65.6–83.5)
60 months	72.9 (53.5–85.3)	71.4 (60.4–79.9)
72 months	67.7 (46.8–81.9)	64.2 (52.1–74.0)
84 months	67.7 (46.8–81.9)	64.2 (52.1–74.0)

Overall survival was defined as the time in months from date of disease progression to the date of death due to any cause or the end of follow-up.

CI, confidence interval; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; OS, overall survival; UIP, usual interstitial pneumonia.

Supplementary Table S8. Univariate Cox regression analysis demonstrating mortality according to patient age, gender, FVC at baseline, and decline in lung function

Parameter	Reference	Number of observations	HR (95% CI)	p-value
FVC% at inclusion	<70%	131	1.53 (0.78–3.00)	0.2140
Decline in FVC% ≥10%	Yes	155	1.77 (0.83–3.74)	0.1383
Decline in FVC of 5%–<10% plus worsening of respiratory symptoms or increased extent of fibrosis on HRCT	Yes	155	0.69 (0.31–1.51)	0.3505
Diagnosis[1]	uILD + IIP + HP	155	3.37 (1.62–6.99)	0.0011
Categorised age	≥50	155	3.77 (1.16–12.28)	0.0276
Sex	Female	155	0.79 (0.41–1.51)	0.4759
UIP-like pattern on HRCT at baseline	Non-UIP-like	155	0.98 (0.47–2.02)	0.9488
DL_{CO} (%) at inclusion	<40%	127	0.95 (0.47–1.94)	0.8903

[1]Patients from the 'Other ILD and sarcoidosis' subgroup were excluded from this analysis.

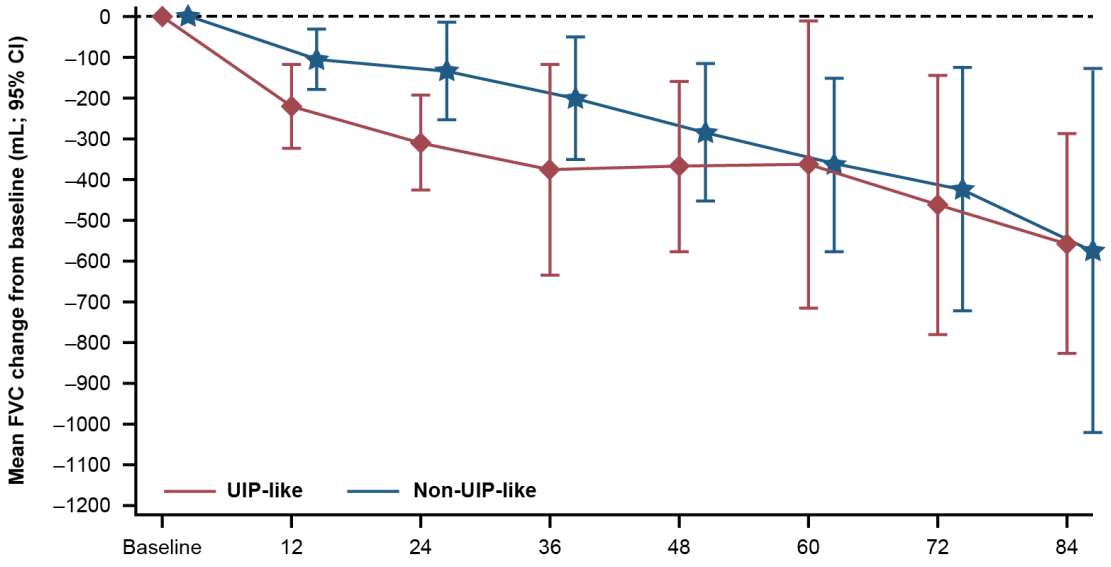
CI, confidence interval; DL_{CO}, diffusing capacity of the lung for carbon monoxide; FVC, forced vital capacity; HP, hypersensitivity pneumonitis; HR, hazard ratio; HRCT, high-resolution computed tomography; IIP, idiopathic interstitial pneumonia; uILD, unclassifiable interstitial lung disease; UIP, usual interstitial pneumonia.

Supplementary Table S9. Factors associated with mortality (multivariate Cox model) without censoring patents who initiated an antifibrotic therapy during the study period (sensitivity analysis)

Parameter	Reference	Number of observations	HR (95% CI)	p-value
FVC% at inclusion	<70%	131	1.85 (0.94–3.66)	0.0754
Decline in FVC of ≥10%	Yes	131	2.46 (1.07–5.66)	0.0351
Diagnosis	Unclassifiable ILD or IIP or HP vs autoimmune ILD	131	3.08 (1.42–6.67)	0.0043
Categorised age	≥50 years	131	4.92 (1.49–16.19)	0.0088

CI, confidence interval; FVC, forced vital capacity; HP, hypersensitivity pneumonitis; HR, hazard ratio; IIP, idiopathic interstitial pneumonia; ILD, interstitial lung disease.

Supplementary Figure S1. Decline from baseline in forced vital capacity according to UIP-like fibrotic pattern on HRCT at baseline



Number of patients at risk								
Non-UIP-like fibrotic pattern	97	83	66	49	41	31	23	12
UIP-like fibrotic pattern	38	31	26	16	13	10	7	4

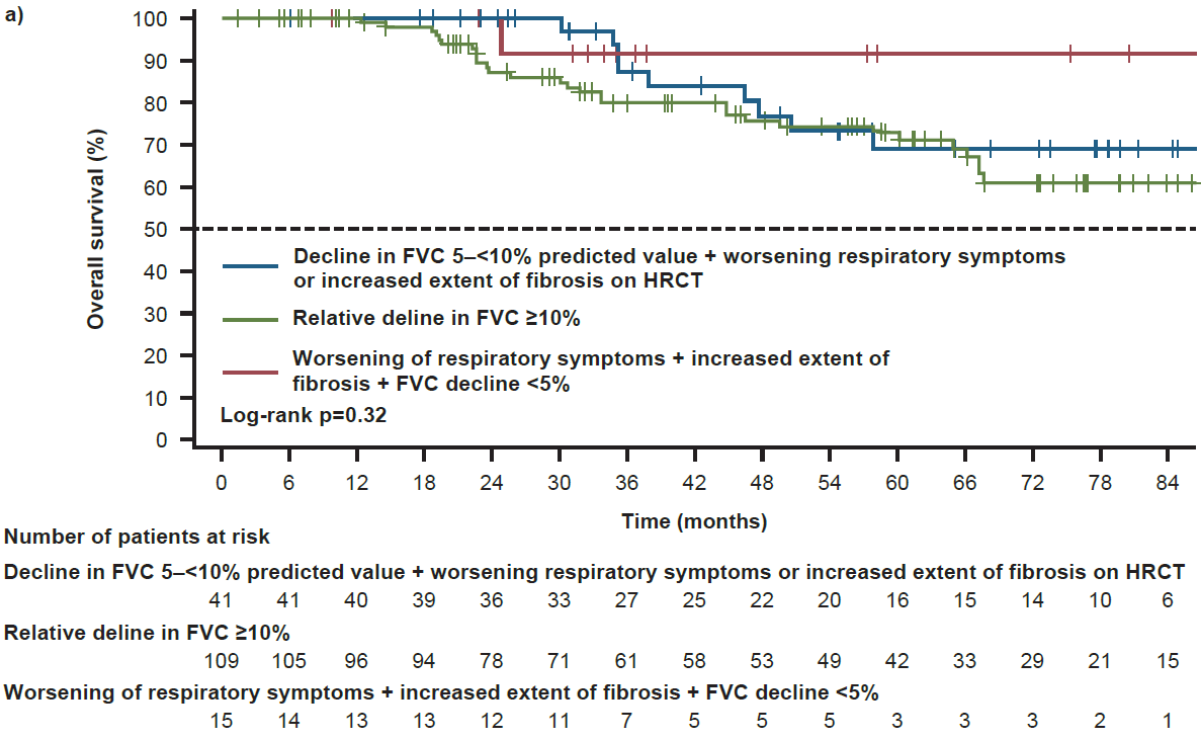
For FVC decline, as the time intervals between measurements varied between subjects, time points were set at 12, 24, 36, 48, 60, 72 and 84 months, and FVC measurements were attributed to those time points using a ±6 months window, using the nearest measurement to the specific time point for analysis.

CI, confidence interval; FVC, forced vital capacity; HRCT, high-resolution computed tomography; UIP, usual interstitial pneumonia.

Supplementary Figure S2

Survival estimates were performed using the Kaplan–Meier method according to patient subgroups by FVC decline (a), and GAP index Stage (b) and compared by log-rank test. Baseline was defined as the date of disease progression. Patients were censored at the time of last clinic visit, lung transplantation for ILD, or initiation of antifibrotic treatment.

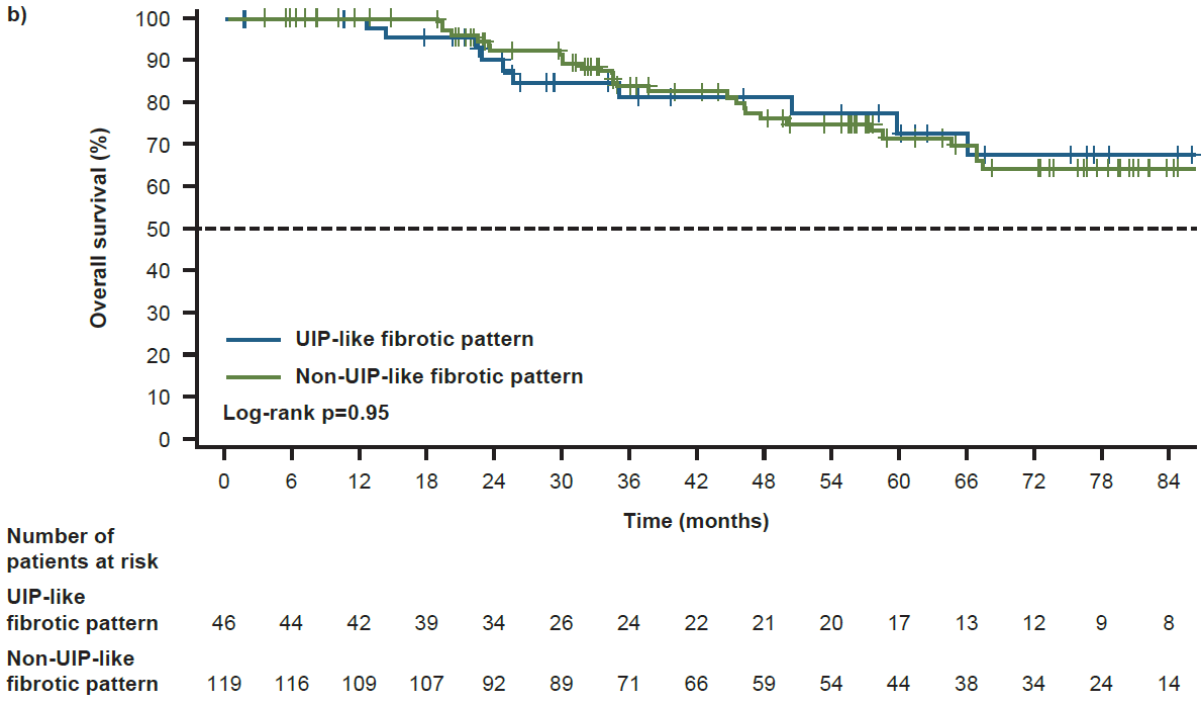
a) Overall survival according to the criteria of progression at baseline



Number of patients at risk

Decline in FVC 5–<10% predicted value + worsening respiratory symptoms or increased extent of fibrosis on HRCT	41	41	40	39	36	33	27	25	22	20	16	15	14	10	6
Relative deline in FVC ≥10%	109	105	96	94	78	71	61	58	53	49	42	33	29	21	15
Worsening of respiratory symptoms + increased extent of fibrosis + FVC decline <5%	15	14	13	13	12	11	7	5	5	5	3	3	3	2	1

b) Overall survival according to UIP-like fibrotic pattern on HRCT at baseline



Number of patients at risk															
UIP-like fibrotic pattern	46	44	42	39	34	26	24	22	21	20	17	13	12	9	8
Non-UIP-like fibrotic pattern	119	116	109	107	92	89	71	66	59	54	44	38	34	24	14

FVC, forced vital capacity; GAP, Gender, Age and Physiology; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; UIP, usual interstitial pneumonia.