

Supplemental Table S1.

| Cause | IPF* (n=22) |
|--|-------------|
| Discontinuation for adverse event or emerging complications | 4 |
| Cardiac disease | 1 |
| Kidney injury | 1 |
| Rash | 1 |
| Lung injury | 1 |
| Patient's request owing to concerns regarding side effects | 6 |
| Social problem ¹ | 2 |
| The medical judgment of the attending physician ² | 4 |
| Others ³ | 6 |

Supplemental Table S1. The reason for no antifibrotic therapy in IPF patients during the study period.

¹ Financial burden.

² Considered elderly.

³ Unknown or unable to confirm whether options for antifibrotic agents were presented.

*Abbreviations: IPF, idiopathic pulmonary fibrosis.

Supplemental Table S2.

| | PF-ILD* | | | | | | | |
|-------------------|-----------------|------------------------|-----------------------------------|-------------|------------------|------------------------|--------------------------------|------------|
| | IPF | | | | Non-IPF | | | |
| | Total (n=64) | Antifibrotic (n=42) | Without antifibrotic (n=22) | P value§ | Total (n=103) | Antifibrotic (n=34) | Without antifibrotic (n=69) | P value |
| Glucocorticoids | 22 (34.38) | 10 (23.81) | 12 (54.55) | 0.0139 | 61 (59.22) | 16 (47.06) | 45 (65.22) | 0.0911 |
| Immunosuppressant | 5 (7.81) | 1 (2.38) | 4 (18.18) | 0.0437 | 22 (21.36) | 7 (20.59) | 15 (21.74) | 1.000 |

Supplemental Table S2. Immunosuppressive agents received during the study period in IPF and non-IPF.

‡Data are shown as n (%).

§Differences were assessed using the χ^2 test or Fisher's exact test, as appropriate.

*Abbreviations: PF-ILD, progressive fibrosing interstitial lung disease; IPF, idiopathic pulmonary fibrosis.

Supplemental Table S3.

| | PF-ILD* | | Non-IPF (n=103) | | | | | | P value§ |
|-------------------|------------------|---------------|--|--|---------------|--------------|------------------------------|---------|----------|
| | Total (n=167) | IPF (n=64) | IIPs other than IPF (n=49) NSIP (n=19), PPFE (n=2) Unclassified (n=26), COP (n=2) | CTD-ILD (n=31) SSc (n=12), RA (n=8), IM ¹ (n=7), Others ² (n=4) | IPAF (n=7) | HP (n=10) | Others ³ (n=6) | | |
| Glucocorticoids | 83 (49.7) | 22 (34.38) | 26 (53.06) | 24 (77.42) | 4 (57.14) | 6 (60.0) | 1 (16.66) | 0.0011 | |
| Immunosuppressant | 27 (16.17) | 5 (7.81) | 7 (14.29) | 14 (45.16) | 1 (14.29) | 0 (0.0) | 0 (0.0) | <0.0001 | |

Supplemental Table S3. Immunosuppressive agents received during the study period in each disease groups.¹Dermatomyositis (n=4), Polymyositis (n=3)²Microscopic Polyangiitis (n=2), Mixed Connective Tissue Disease (n=1), Systemic lupus erythematosus (n=1).³Exposure-related ILD (n=5), Sarcoidosis (n=1)[‡]Data are shown as n (%).§Differences were assessed using the χ^2 test or Fisher's exact test, as appropriate.

Abbreviations: PF-ILD, progressive fibrosing interstitial lung disease; IPF, idiopathic pulmonary fibrosis; IIPs, idiopathic interstitial pneumonias; NSIP, non-specific interstitial pneumonia; PPFE, pleuroparenchymal fibroelastosis; COP, cryptogenic organizing pneumonia; CTD-ILD, connective tissue disease-interstitial lung disease; SSc, systemic sclerosis; IM, inflammatory myopathies; RA, rheumatoid arthritis; IPAF, interstitial pneumonia with autoimmune features; HP, hypersensitivity pneumonitis.

Supplemental Table S4.

| Immunosuppressant | IPF* (n=5) | Non-IPF (n=22) |
|-----------------------|------------|----------------|
| Cyclosporine A | 5 | 12 |
| Mycophenolate mofetil | 0 | 9 |
| Cyclophosphamide | 1 | 3 |
| Tacrolimus | 0 | 3 |
| Azathioprine | 0 | 2 |
| Tocilizumab | 0 | 3 |

| | Glucocorticoid | Cyclosporine A | Mycophenolate mofetil | Cyclophosphamide | Tacrolimus | Azathioprine | Tocilizumab |
|---------------------------------------|----------------|----------------|-----------------------|------------------|------------|--------------|-------------|
| Systemic sclerosis (n=12) | 10 | 1 | 7 | 2 | 0 | 1 | 3 |
| Rheumatoid arthritis (n=8) | 5 | 2 | 0 | 0 | 0 | 0 | 0 |
| Dermatomyositis (n=4) | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| Polymyositis (n=3) | 3 | 1 | 0 | 0 | 1 | 0 | 0 |
| Microscopic Polyangiitis (n=2) | 2 | 0 | 0 | 1 | 0 | 0 | 0 |
| Mixed Connective Tissue Disease (n=1) | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Systemic lupus erythematosus (n=1) | 1 | 1 | 0 | 0 | 0 | 0 | 0 |

Supplemental Table S4. The details of immunosuppressant received during the study period in IPF and non-IPF, CTD-ILDs.

*Abbreviations: IPF, idiopathic pulmonary fibrosis; CTD-ILD, connective tissue disease-interstitial lung disease.

Supplemental Table S5.

| | Excluded | PF-ILD* | | |
|---|---------------------|------------------------|---------------------|----------|
| | Non-PF-ILD (n=383) | Low %FVC (<45%) (n=20) | Total (n=167) | P value§ |
| Characteristics | | | | |
| Sex, male | 205 (53.51) ‡ | 11 (55.0) | 115 (68.86) | 0.0035 |
| Age (years) | 68 (61.0-74.0) | 52 (43.25-65.25) | 68.5 (62.5-72.0) | <0.0001 |
| BMI | 22.76 (20.89-24.85) | 23.20 (19.46-25.83) | 22.84 (21.22-25.33) | 0.8181 |
| COPD | 58 (15.85) | 0 (0.0) | 20 (13.07) | 0.1385 |
| DM | 90 (24.66) | 3 (16.67) | 24 (14.37) | 0.1112 |
| CTD-ILD | 144 (37.6) | 7 (35.00) | 31 (18.56) | <0.001 |
| Serological examination | | | | |
| Monocyte count | 401.3 (300-520.6) | 456.5 (329.4-571.4) | 400.8 (319.5-508.3) | 0.6033 |
| LDH | 210 (183-245.8) | 253 (211.5-336.8) | 219 (192-246.5) | 0.0078 |
| KL-6 | 658 (389.8-1126.3) | 1115 (791.18-3363.3) | 922 (510-1310) | <0.0001 |
| CRP | 0.04 (0.1-0.32) | 0.33 (0.11-0.44) | 0.13 (0.05-0.35) | 0.1690 |
| Pulmonary function | | | | |
| FVC | 2.6 (1.97-3.22) | 1.36 (1.05-1.52) | 2.61 (2.08-3.14) | <0.0001 |
| %FVC | 86.4 (71.9-92.9) | 38.75 (34.48-42.55) | 83.3 (71.9-92.9) | <0.0001 |
| DLCO (n=402) | 10.93 (8.05-14.74) | 3.95 (1.73-6.59) | 10.07 (7.47-12.0) | <0.0001 |
| %DLCO (n=402) | 66.5 (48.2-82.1) | 20.2 (10.35-35.75) | 61.75 (47.8-76.32) | <0.0001 |
| Radiological findings | | | | |
| Honeycombing | 70 (18.28) | 4 (20.0) | 65 (38.92) | <0.0001 |
| Traction bronchiectasis | 170 (44.39) | 12 (60.0) | 101 (60.48) | 0.0010 |
| Immunosuppressive agents during the study period | | | | |
| Glucocorticoids | 192 (50.13) | 15 (75.0) | 82 (49.1) | <0.0001 |
| Immunosuppressant | 115 (30.03) | 12 (60.0) | 28 (16.77) | <0.0001 |
| Outcome | | | | |
| Death | 35 (9.49) | 2 (10.53) | 52 (31.14) | <0.001 |

Supplemental Table S5. Characteristics of excluded patients and PF-ILD patients at first visit.

‡Data are shown as n (%) or median (interquartile range).

§Differences among continuous variables were assessed using the Kruskal-Wallis test; differences among categorical variables were assessed using the χ^2 test or Fisher's exact test, as appropriate. The Steel-Dwass test for multiple comparisons was used for statistical analyses of three or more groups.

*Abbreviations: PF-ILD, progressive fibrosing interstitial lung disease; IPF, idiopathic pulmonary fibrosis; IIPs, idiopathic interstitial pneumonias; CTD-ILD, connective tissue disease-interstitial lung disease; IPAf, interstitial pneumonia with autoimmune features; HP, hypersensitivity pneumonitis; BMI, body mass index; COPD, chronic obstructive lung pulmonary disease; DM, diabetes mellitus; LDH, lactate dehydrogenase; KL-6, sialylated carbohydrate antigen Krebs von den Lungen-6; CRP, C-reactive protein; FVC, forced vital capacity; DLCO, diffusing capacity for carbon monoxide.

Supplemental Table S6.

| Lacking pulmonary function test after PF-ILD diagnosis (n=12) | Excluded | | | PF-ILD* | | | | | | |
|---|-------------------------|-------------------------|-------------------------|------------------------|--------------------------|--------------|------------------------|------------------------|------------------------|--------|
| | Total (n=155) | IPF | | | Non-IPF | | | P value | | |
| | | Total (n=61) | Antifibrotic (n=42) | No-antifibrotic (n=19) | P value § | Total (n=94) | Antifibrotic (n=34) | No-antifibrotic (n=60) | | |
| Characteristics | | | | | | | | | | |
| Sex, male | 10 (83.33)‡ | 105 (67.74) | 45 (73.77) | 29 (69.05) | 16 (84.21) | 0.3464 | 60 (63.83) | 24 (70.59) | 36 (60.0) | 0.5007 |
| Age (years) | 71.0 (62.5-74.25) | 71.0 (64.0-75.0) | 73.0 (68.5-77.0) | 71.5 (66.75-76.25) | 74 (71.0-78.0) | 0.1467 | 69 (60.8-74.0) | 69.5 (63.25-74) | 69 (62.5-74.0) | 0.6086 |
| BMI | 22.36 (21.70-24.81) | 22.83 (21.13-25.39) | 23.73 (21.77-26.31) | 23.81 (21.63-26.71) | 23.36 (21.83-25.39) | 0.8274 | 22.45 (20.21-25.07) | 23.57 (20.98-26.47) | 21.91 (19.86-24.26) | 0.0156 |
| COPD | 3 (25.00) | 21 (13.54) | 7 (14.06) | 5 (11.9) | 2 (10.53) | 0.8816 | 14 (12.62) | 7 (20.59) | 7 (11.48) | 0.2341 |
| DM | 0 (0.00) | 24 (15.48) | 11 (17.19) | 5 (11.9) | 6 (31.58) | 0.1216 | 13 (12.62) | 3 (8.82) | 10 (14.49) | 0.7168 |
| Serological examination | | | | | | | | | | |
| Monocyte count | 336 (286.4-693.4) | 432.9 (337.9-539) | 420.5 (333.3-527.1) | 402.6 (329.67-539) | 439.1 (339.8-498.4) | 0.8292 | 433.2 (340.7-552) | 437.7 (379.8-554.7) | 429.2 (302.1-551.5) | 0.3584 |
| LDH | 218.5 (161.5-259.3) | 217 (194.5-250.3) | 216 (193.5-260.0) | 214 (192-248) | 217 (196.5-274) | 0.5564 | 217.5 (193.8-245.5) | 213 (181.5-246.5) | 224.5 (200.5-250.3) | 0.3037 |
| KL-6 | 647.5 (403.2-1496.8) | 898.5 (590.7-1357.2) | 948.3 (700.4-1554.8) | 916.4 (740.5-1606) | 1058.9 (614.5-1510.6) | 0.9645 | 852 (564-1269) | 829 (598.6-1423.1) | 871 (464.1-1166.6) | 0.2519 |
| CRP | 0.30 (0.1-1.28) | 0.16 (0.1-0.36) | 0.16 (0.1-0.43) | 0.16 (0.1-0.32) | 0.19 (0.11-0.46) | 0.4010 | 0.15 (0.1-0.35) | 0.18 (0.1-0.35) | 0.14 (0.07-0.35) | 0.5074 |
| Pulmonary function | | | | | | | | | | |
| FVC | 2.13 (1.72-2.57) | 2.31 (1.81-2.85) | 2.29 (1.91-2.84) | 2.29 (1.89-2.87) | 2.35 (1.91-2.83) | 0.9438 | 2.33 (1.79-2.89) | 2.33 (1.96-2.77) | 2.41 (1.75-3.07) | 0.6193 |
| %FVC | 84.15 (72.7-92.78) | 82.1 (68.0-91.6) | 84.3 (71.8-93.15) | 86.55 (72.83-94.0) | 84.1 (68.9-91.7) | 0.2916 | 78.8 (65.1-90.4) | 79.3 (63.0-90.75) | 79.2 (65.6-89.6) | 0.5710 |
| DLCO (n=125) | 9.51 (3.64-15.26) | 10.07 (7.47-12.0) | 9.96 (7.88-12.0) | 11.04 (8.41-12.74) | 8.47 (7.07-10.36) | 0.0226 | 10.07 (7.33-11.98) | 9.69 (7.26-11.76) | 10.29 (7.49-12.64) | 0.6082 |
| %DLCO (n=125) | 64.26 (20.20-79.85) | 58.5 (44.6-75.1) | 59.17 (46.65-77.44) | 69.66 (49.05-80.97) | 47.8 (41.4-57.77) | 0.0280 | 58.5 (42.95-72.8) | 52.8 (40.03-71.75) | 61.5 (43.73-74.68) | 0.2074 |
| Radiological findings | | | | | | | | | | |
| Honeycombing | 6 (50.0) | 59 (38.06) | 34 (55.74) | 22 (52.38) | 12 (63.16) | 0.5792 | 25 (26.6) | 12 (35.29) | 13 (21.67) | 0.1452 |
| Traction bronchiectasis | 5 (41.67) | 96 (61.94) | 39 (63.93) | 27 (64.29) | 12 (63.16) | 1.000 | 57 (58.25) | 22 (64.71) | 35 (58.33) | 0.6614 |
| Immunosuppressive agents | | | | | | | | | | |
| Glucocorticoids (PSL<10mg/day) | 1 (8.33) | 11 (7.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1.000 | 11 (11.70) | 3 (8.82) | 8 (13.33) | 0.7414 |
| Glucocorticoids (PSL≥10mg/day) | 5 (41.67) | 18 (11.67) | 6 (9.84) | 4 (9.52) | 2 (10.53) | 1.000 | 12 (12.77) | 5 (14.71) | 7 (11.67) | 0.7515 |
| Immunosuppressant | 1 (8.33) | 15 (9.68) | 2 (3.28) | 1 (2.38) | 1 (5.36) | 0.5295 | 13 (13.83) | 6 (17.65) | 7 (11.67) | 0.5360 |

Supplemental Table S6. Baseline characteristics of patients with PF-ILD between the antifibrotic and no antifibrotic group at PF-ILD diagnosis and except the patients with lacking PFTs after PF-ILD diagnosis.

‡Data are shown as n (%) or median (interquartile range).

§Differences among continuous variables were assessed using Welch's t-test for monocyte count and pulmonary function tests (PFTs) and the Wilcoxon rank sum test for other variables; differences among categorical variables were assessed using the χ^2 test or Fisher's exact test, as appropriate.

*Abbreviations: PF-ILD, progressive fibrosing interstitial lung disease; IPF, idiopathic pulmonary fibrosis; BMI, body mass index; COPD, chronic obstructive lung pulmonary disease; DM, diabetes mellitus; LDH, lactate dehydrogenase; KL-6, sialylated carbohydrate antigen Krebs von den Lungen-6; CRP, C-reactive protein; FVC, forced vital capacity; DLCO, diffusing capacity for carbon monoxide; PSL, prednisolone.

Supplemental Table S7.

| | PF-ILD* | | | | | | | | P value§ |
|----------------------------------|------------------|---------------|--|--|---------------|--------------|------------------------------|--------|----------|
| | Total (n=167) | IPF (n=64) | Non-IPF (n=103) | | | | | | |
| | | | IIPs other than IPF (n=49) NSIP (n=19), PPFE (n=2) Unclassified (n=26), COP (n=2) | CTD-ILD (n=31), SSc (n=12), RA (n=8), IM ¹ (n=7), Others ² (n=4) | IPAF (n=7) | HP (n=10) | Others ³ (n=6) | | |
| Total death | 52 (31.14) ‡ | 22 (34.38) | 17 (34.69) | 8 (25.81) | 2 (28.57) | 3 (30.0) | 0 (0.00) | 0.6287 | |
| Respiratory failure ⁴ | 35 (23.44) | 15 (23.44) | 12 (24.49) | 4 (12.90) | 1 (14.29) | 3 (30.0) | 0 (0.00) | 0.6029 | |
| Lung cancer | 4 (2.4) | 1 (1.56) | 2 (4.08) | 0 (0.00) | 1 (14.29) | 0 (0.00) | 0 (0.00) | 0.2861 | |
| Others | 5 (2.99) | 1 (1.56) | 1 (2.04) | 3 (9.68) ⁵ | 0 (0.00) | 0 (0.00) | 0 (0.00) | 0.3871 | |
| Unknown | 8 (4.79) | 5 (7.81) | 2 (3.92) | 1 (3.23) | 0 (0.00) | 0 (0.00) | 0 (0.00) | 0.9157 | |

Supplemental Table S7. The cause of death in each disease groups.¹Dermatomyositis (n=4), Polymyositis (n=3)²Microscopic Polyangiitis (n=2), Mixed Connective Tissue Disease (n=1), Systemic lupus erythematosus (n=1).³Exposure-related ILD (n=5), Sarcoidosis (n=1)⁴Respiratory failure was defined as a disease progression, acute exacerbation, and complication of ILD other than lung cancer (e.g pneumothorax).⁵Colon cancer (n=1), Heart failure (n=1), infection (n=1)

‡Data are shown as n (%).

§Differences among continuous variables were assessed using the one-way analysis of variance; differences among categorical variables were assessed using the χ^2 test or Fisher's exact test, as appropriate.

*Abbreviations: IPF, idiopathic pulmonary fibrosis; IIPs, idiopathic interstitial pneumonias; NSIP, non-specific interstitial pneumonia; PPFE, pleuroparenchymal fibroelastosis; COP, cryptogenic organizing pneumonia; CTD-ILD, connective tissue disease-interstitial lung disease; SSc, systemic sclerosis; IM, inflammatory myopathies; RA, rheumatoid arthritis; IPAF, interstitial pneumonia with autoimmune features; HP, hypersensitivity pneumonitis.

Supplemental Table S8.

| Antifibrotic agents | IPF* (n=42) | non-IPF (n=34) |
|---------------------|-------------|----------------|
| Nintedanib | 17 | 20 |
| Pirfenidone | 25 | 14 |

Supplemental Table S8. The prescription between nintedanib and pirfenidone in each group.

*Abbreviations: IPF, idiopathic pulmonary fibrosis.