Supplementary Material

Table S1: Patients' clinical characteristics			
Variables	ILD	Healthy control	*P*-value
Number	91	71	-
Age (years)	55 (45–64)[a]	52 (48–55)[a]	0.176[b]
SP-A	42.9 (32.5–65.3)[a]	20.1 (15.1–24.6)[a]	<0.001[b]
KL-6	1192 (764–2312)[a]	194 (156–289)[a]	<0.001[b]

[a]IQR; [b]*P*-value was calculated by Mann–Whitney U test.
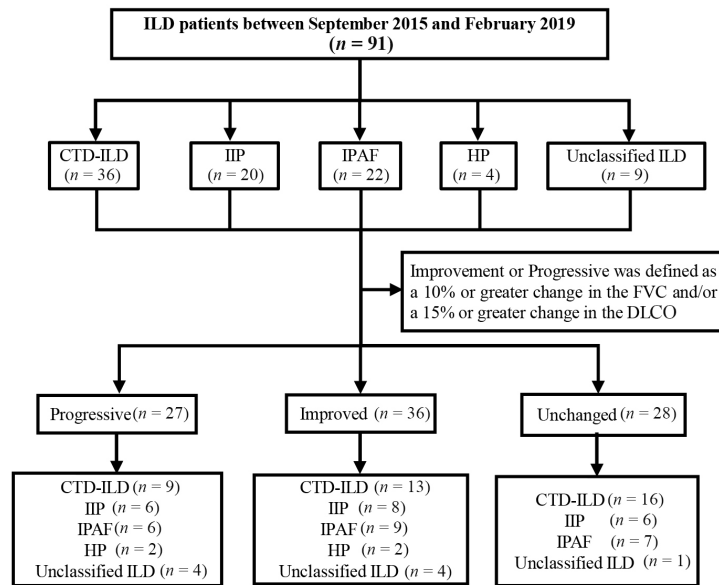
ILD: interstitial lung disease; IQR: interquartile range; KL-6: Krebs von den Lungen-6; SP-A: surfactant protein-A.

| Table S2: Serum SP-A and KL-6 levels in patients with pathological types of ILDs Pretreatment and Post-treatment. Others: patients with HP or with unclassified ILD					
Variables	CTD-ILD	IIP	IPAF	Others	*P*-value
Number (%)	36 (39.56%)	20 (21.98%)	22 (24.18%)	13 (14.29%)	-
SP-A					
Pretreatment	46.7 (36.8–68.3)[a]	40.2 (31.1–51.7)[a]	44.1 (29.6–64.6)[a]	46.3 (32.8–102.6)[a]	0.298[b]
Post-treatment	46.7 (31.1–63.9)[a]	40.0 (31.1–64.4)[a]	34.2 (21.2–56.7)[a]	49.5 (39.2–76.4)[a]	0.347[b]
KL-6					
Pretreatment	1246.5 (847–2333.7)[a]	1052.0 (745–1502.2)[a]	1073.0 (702.2–2046.0)[a]	1246.0 (665.0–3009.5)[a]	0.320[b]
Post-treatment	1321.5 (697.5–2616.7)[a]	735 (514.7–1437.7)[a]	742.0 (459.5–1676.5)[a]	1463.0 (661.0–3837.0)[a]	0.136[b]

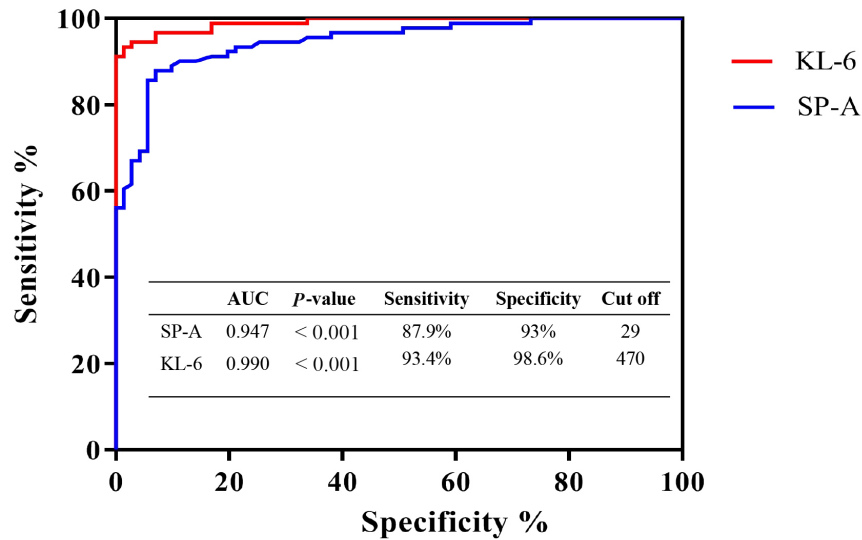[a]IQR; [b]*P*-value was calculated by Kruskal–Wallis test.

CTD-ILD: connective tissue disease associated with ILD; HP: hypersensitivity pneumonitis; IIP: idiopathic interstitial pneumonia; ILD: interstitial lung disease; IPAF: interstitial pneumonia with autoimmune features; IQR: interquartile range; KL-6: Krebs von den Lungen-6; SP-A: surfactant protein-A.
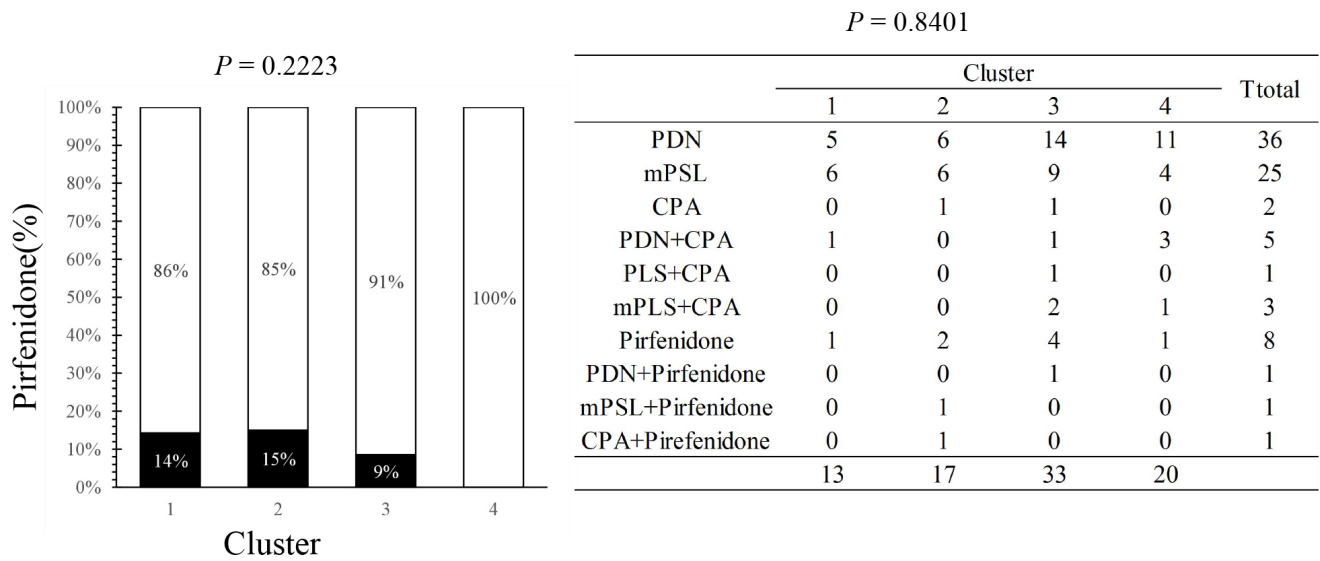
Figure S1: Flowchart for the patients with ILD included in the study and their allocation into the three study groups. ILD: interstitial lung disease; DLCO: diffusing capacity for carbon monoxide; FVC: forced vital capacity; HP: hypersensitivity pneumonitis; CTD-ILD: connective tissue disease associated with ILD; IIP: idiopathic interstitial pneumonia; IPAF: interstitial pneumonia with autoimmune features.
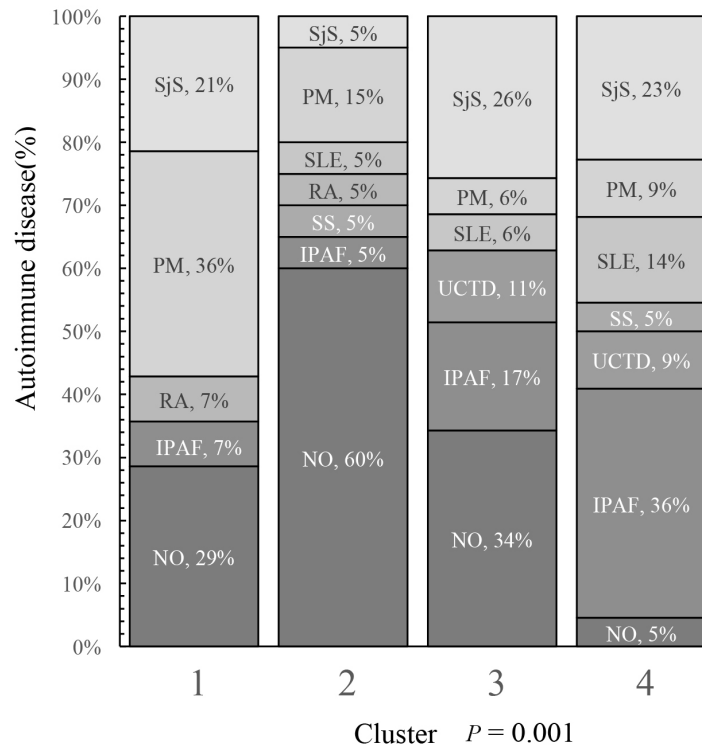
Figure S2: Treatment of different kinds of autoimmune diseases in the cluster analysis. *P*-values were calculated by Fisher's exact test. SjS: Sjogren's syndrome; PM: polymyositis dermatomyositis; DM: dermatomyositis; RA: rheumatoid arthritis; SS: systemic sclerosis; SLE: systemic lupus erythematosus; UCTD: undifferentiated connective tissue disease; NO: without autoimmune disease. Comparison of serum KL-6 and SP-A levels between ILD patients and healthy volunteers. We used ROC curve analysis to evaluate the sensitivity and specificity of serum KL-6 and SP-A concentrations as biomarkers for the diagnosis of ILD in Figure S3. Based on the area under the ROC curve (AUC), when the cutoff level for SP-A to distinguish ILD was 29 ng/mL, the sensitivity and specificity were 87.9% and 93%, respectively (AUC = 0.947, 95% CI = 0.914–0.979). When the cutoff level for KL-6 to distinguish IPAF was 470 U/mL, the sensitivity and specificity were 93.4% and 98.6%, respectively (AUC = 0.990, 95% CI = 0.980–1.000).

	AUC	*P*-value	Sensitivity	Specificity	Cut off
SP-A	0.947	< 0.001	87.9%	93%	29
KL-6	0.990	< 0.001	93.4%	98.6%	470

Figure S3: Receiver-operating characteristic (ROC) curve according to the specificity and sensitivity of serum SP-A and KL-6 levels. SP-A: surfactant protein-A; KL-6: Krebs von den Lungen-6. Of the 83 cases included in the cluster analysis, 61 were treated with steroids alone (prednisolone [PDN]) and methylprednisolone (mPSL) steroids alone. Only eight patients were treated with antifibrotic therapy alone. There was no significant difference (*P* = 0.8401) in the ratio of antifibrotic therapy among the clusters (Figure S4). Therefore, we consider that the relationship between the change of SP-A and KL-6 levels and the treatment response of this study is mainly response to steroids.

$P = 0.8401$

	Cluster				T total
	1	2	3	4	
PDN	5	6	14	11	36
mPSL	6	6	9	4	25
CPA	0	1	1	0	2
PDN+CPA	1	0	1	3	5
PLS+CPA	0	0	1	0	1
mPLS+CPA	0	0	2	1	3
Pirfenidone	1	2	4	1	8
PDN+Pirfenidone	0	0	1	0	1
mPSL+Pirfenidone	0	1	0	0	1
CPA+Pirefenidone	0	1	0	0	1
	13	17	33	20	

Figure S4: Treatment of three groups in the cluster analysis. *P*-values were calculated by Fisher's exact test. PDN: prednisone; mPSL: methylprednisolone; CPA: cyclophosphamide; PLS: prednisolone.