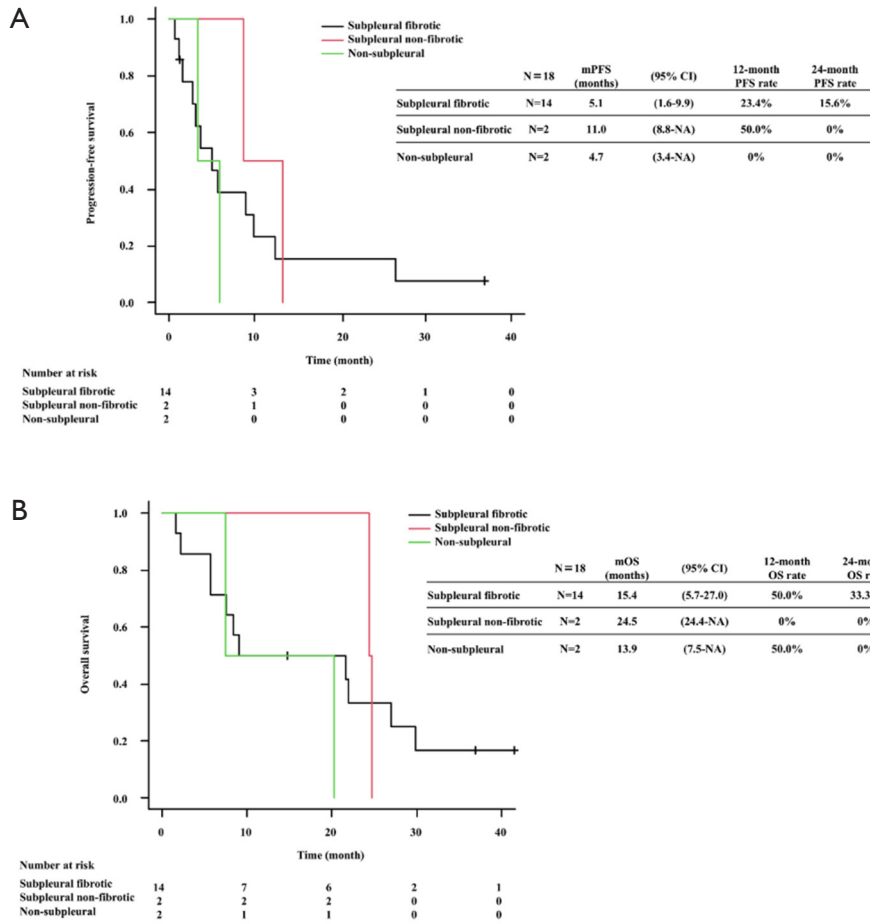


**Figure S1** Progression-free survival (A) and overall survival (B) in patients with NSCLC and ILA treated with ICI. ICI, immune checkpoint inhibitor; ILA, interstitial lung abnormalities; NSCLC, non-small cell lung cancer.



**Figure S2** Progression-free survival (A) and overall survival (B) in patients with NSCLC and ILA treated with ICI, classified by radiologic pattern. NSCLC, non-small cell lung cancer; ICI, immune checkpoint inhibitor; ILA, interstitial lung abnormalities.

**Table S1** Treatment regimen detail in patients with IIPs

| Treatment              | Regimens                       | n (%)     |
|------------------------|--------------------------------|-----------|
| Chemo-ICI (n=6)        | CDDP/CBDCA+PEM+Pembrolizumab   | 4 (66.6)  |
|                        | CDDP/CBDCA+PEM+Atezolizumab    | 1 (16.7)  |
|                        | CBDCA+PTX/nabPTX+Pembrolizumab | 1 (16.7)  |
| ICI monotherapy (n=47) | Pembrolizumab                  | 19 (40.4) |
|                        | Nivolumab                      | 20 (42.6) |
|                        | Atezolizumab                   | 8 (17.0)  |

IIPs, idiopathic interstitial pneumonias; ICI, immune checkpoint inhibitor; CDDP, cisplatin; CBDCA, carboplatin; PEM, pemetrexed; PTX, paclitaxel; nabPTX, nanoparticle albumin-bound paclitaxel.

**Table S2** Antitumor response in patients with IIPs

| Tumor response        | Chemo-ICI (n=6), n (%) | ICI monotherapy (n=47), n (%) |
|-----------------------|------------------------|-------------------------------|
| ORR                   | 4 (66.6)               | 15 (31.9)                     |
| DCR                   | 4 (66.6)               | 26 (55.3)                     |
| Best overall response |                        |                               |
| CR                    | 0 0                    | 0 0                           |
| PR                    | 4 (66.6)               | 15 (31.9)                     |
| SD                    | 0 0                    | 11 (23.4)                     |
| PD                    | 2 (33.4)               | 16 (34.0)                     |
| NE                    | 0 0                    | 5 (10.7)                      |

IIPs, idiopathic interstitial pneumonias; ICI, immune checkpoint inhibitor; ORR, overall response rate; DCR, disease control rate; CR, complete response; PR, partial response; SD, stable disease; PD, Progressive disease; NE, not evaluable.

**Table S3** Details of immune related adverse events other than pneumonitis

| Adverse events, n (%)                              | Chemo-ICI (n=6) | ICI monotherapy (n=47) |
|--|-----------------|------------------------|
| Liver dysfunction                                  |                 |                        |
| Grade 1  | 0               | 1 (2.1)                |
| Grade 3  | 1 (16.7)        | 1 (2.1)                |
| Grade 4  | 1 (16.7)        | 0                      |
| Hypothyroidism                                     |                 |                        |
| Grade 1  | 0               | 2 (4.2)                |
| Grade 2  | 0               | 1 (2.1)                |
| Adrenal insufficiency                              |                 |                        |
| Grade 1  | 0               | 1 (2.1)                |
| Grade 3  | 0               | 1 (2.1)                |
| Rash   |                 |                        |
| Grade 1  | 0               | 1 (2.1)                |
| Grade 2  | 0               | 1 (2.1)                |
| Grade 3  | 0               | 2 (4.2)                |
| Diarrhea   |                 |                        |
| Grade 1  | 0               | 1 (2.1)                |
| Grade 2  | 0               | 2 (4.2)                |
| Colitis grade 1                                    | 0               | 1 (2.1)                |
| Peripheral neuropathy grade 4                      | 0               | 1 (2.1)                |
| Adrenal insufficiency grade 3 and diarrhea grade 3 | 0               | 1 (2.1)                |

ICI, immune checkpoint inhibitor.

**Table S4** Status of long responder in patients with IIPs

| Age/gender | Histology | Stage      | PD-L1   | %FVC    | %DL <sub>co</sub> | Radiologic Pattern | Honeycomb | Treatment line | Regimen       | ORR | Pneumonitis | irAE                     |
|------------|-----------|------------|---------|---------|-------------------|--------------------|-----------|----------------|---------------|-----|-------------|--------------------------|
| 82M        | Ad        | IVB        | 1-49%   | Unknown | Unknown           | Probable UIP       | Absent    | 2nd line       | Nivolumab     | SD  | None        | None                     |
| 76M        | Sq        | IIIB       | Unknown | 121     | 72                | Probable UIP       | Absent    | 4th line       | Atezolizumab  | PR  | None        | Liver dysfunction Grade3 |
| 67M        | Sq        | IVA        | >50%    | 80      | 48                | UIP                | Present   | 1st line       | Pembrolizumab | PR  | Grade 1     | Rash Grade2              |
| 71M        | LCNEC     | Recurrence | Unknown | 69      | 11                | UIP                | Present   | 3rd line       | Atezolizumab  | PR  | None        | None                     |
| 62M        | NSCLC     | IVA        | Unknown | 95      | 13                | UIP                | Present   | 3rd line       | Atezolizumab  | PR  | None        | Hypothyroidism Grade1    |

PD-L1, programmed death-ligand 1; %FVC, percent predicted forced vital capacity; %DL<sub>co</sub>, percent predicted diffusing capacity of the lung for carbon monoxide; ORR, overall response rate; Ad, adenocarcinoma; Sq, squamous cell carcinoma; LCNEC, large-cell neuroendocrine carcinoma; NSCLC, non-small cell lung cancer; UIP, usual interstitial pneumonia; PR, partial response; SD, stable disease.

**Table S5** Patient characteristic in patients with ILAs

| Characteristics                        | Total (n=18) |
|--|--------------|
| Age, median [range], y                 | 71 [59–83]   |
| Sex, n (%)                             |              |
| Male                                   | 17 (94.5)    |
| Female                                 | 1 (5.5)      |
| Smoking history, n (%)                 |              |
| Never                                  | 1 (5.5)      |
| Former or current                      | 17 (94.5)    |
| ECOG-PS, n (%)                         |              |
| 0                                      | 5 (27.8)     |
| 1                                      | 11 (61.2)    |
| 2                                      | 2 (11.0)     |
| Stage, n (%)                           |              |
| III                                    | 2 (11.0)     |
| IV                                     | 11 (61.2)    |
| Recurrence                             | 5 (27.8)     |
| Histology, n (%)                       |              |
| Adenocarcinoma                         | 10 (55.6)    |
| Squamous cell carcinoma                | 8 (44.4)     |
| PD-L1 expression [TPS (%)], n (%)      |              |
| <1%                                    | 6 (33.3)     |
| 1–49%                                  | 4 (22.2)     |
| ≥50%                                   | 7 (39.0)     |
| Unknown                                | 1 (5.5)      |
| Treatment Line of ICI, n (%)           |              |
| 1 <sup>st</sup>                        | 12 (66.6)    |
| 2 <sup>nd</sup>                        | 4 (22.2)     |
| 3 <sup>rd</sup> or later               | 2 (11.0)     |
| Treatment regimen, n (%)               |              |
| ICI monotherapy                        | 13 (72.2)    |
| Chemo-ICI                              | 5 (27.8)     |
| Treatment of antifibrotic drugs, n (%) |              |
| Pirfenidone                            | 1 (5.5)      |
| None                                   | 17 (94.5)    |
| EGFR mutation status, n (%)            |              |
| Negative                               | 17 (94.5)    |
| Unknown                                | 1 (5.5)      |

**Table S5** (continued)**Table S5** (continued)

| Characteristics                  | Total (n=18)  |
|----------------------------------|---------------|
| ALK fusion status, n (%)         |               |
| Negative                         | 16 (89.0)     |
| Unknown                          | 2 (11.0)      |
| Radiologic pattern of ILA, n (%) |               |
| Non-subpleural                   | 2 (11.0)      |
| Subpleural non-fibrotic          | 2 (11.0)      |
| Subpleural fibrotic              | 14 (78.0)     |
| %FVC median [range]              | 97.2 [59–120] |
| %DL <sub>CO</sub> median [range] | 67.9 [56–123] |

ILA, interstitial lung abnormalities; PD-L1, programmed death-ligand 1; TPS, tumor proportion score; ICI, immune checkpoint inhibitor; EGFR, epidermal growth factor receptor; ALK, anaplastic lymphoma kinase; %FVC, percent predicted forced vital capacity; %DL<sub>CO</sub>, percent predicted diffusing capacity of the lung for carbon monoxide.

**Table S6** Antitumor response in patients with ILAs

| Tumor response        | Chemo-ICI (n=5), n (%) | ICI monotherapy (n=13), n (%) |
|-----------------------|------------------------|-------------------------------|
| ORR                   | 2 (40.0)               | 7 (53.8)                      |
| DCR                   | 5 (100)                | 11 (84.6)                     |
| Best overall response |                        |                               |
| CR                    | 0                      | 0                             |
| PR                    | 2 (40.0)               | 7 (53.8)                      |
| SD                    | 3 (60.0)               | 4 (30.8)                      |
| PD                    | 0                      | 2 (15.4)                      |
| NE                    | 0                      | 0                             |

ILA, interstitial lung abnormalities; ICI, immune checkpoint inhibitor; ORR, overall response rate; DCR, disease control rate; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; NE, not evaluable.

**Table S7** Pneumonitis for each imaging pattern and treatment regimen with ILAs

| Variables                           | Total (n=18) | Subpleural fibrotic (n=14) | Subpleural non-fibrotic (n=2) | Non-subpleural (n=2) | Chemo-ICI (n=5) | ICI monotherapy (n=13) |
|-------------------------------------|--------------|----------------------------|-------------------------------|----------------------|-----------------|------------------------|
| Pneumonitis                         | 4 (22.2)     | 3 (21.4)                   | 0 (0)                         | 1 (50.0)             | 0 (0)           | 4 (30.7)               |
| Grade 1/2                           | 2 (11.1)     | 1 (7.1)                    | 0 (0)                         | 1 (50.0)             | 0 (0)           | 2 (15.4)               |
| Grade 3/4                           | 2 (11.1)     | 2 (14.3)                   | 0 (0)                         | 0 (0)                | 0 (0)           | 2 (15.4)               |
| Time to onset, days, median [range] | 21 [5–172]   | 21 [5–36]                  | --                            | 172 [--]             | --              | 21 [5–172]             |
| Led to discontinuation              | 3 (16.7)     | 3 (21.4)                   | --                            | 0 (0)                | --              | 3 (23.1)               |

ILA, interstitial lung abnormalities; ICI, immune checkpoint inhibitor.