Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Nishino M, Sholl LM, Hodi FS, et al. Anti–PD-1–related pneumonitis during cancer immunotherapy. N Engl J Med 2015;373:288-90. DOI: 10.1056/NEJMc1505197

Supplementary Appendix

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Table S1. Patient characteristics and clinical course of the 3 cases of anti-PD-1 antibody-related pneumonitis

	PATIENT 1	**PATIENT 2**	**PATIENT 3**
Age/Sex	70/Male	38/Female	58/Male
Trial phase	II	III	I
Agent	Nivolumab given sequentially with ipilimumab	Nivolumab (3 mg/kg)	Nivolumab (1 mg/kg)
Doses given before onset	6 doses of nivolumab (3 mg/kg) followed by 3 doses of ipilimumab (3 mg/kg)	6 doses of nivolumab (3 mg/kg)	4 doses of nivolumab (1 mg/kg)
Onset since therapy start	24.3 weeks	15.3 weeks	7.4 weeks
Toxicity grade of pneumonitis	3	3	2
Respiratory symptoms	Cough, shortness of breath, hypoxia, subacute fever	Dyspnea, hypoxia	Cough with deep inspiration
Treatment for pneumonitis	IV antibiotics, IV steroids, IV infliximab, requiring ICU admission and intubation	IV antibiotics, IV steroids, IV infliximab, requiring ICU admission	Oral steroid (Prednisone), No admission needed. Nivolumab held at dx, restarted after 8 weeks
Outcome	Alive, off trial	Died	Alive, on trial without recurrent pneumonitis

Table S2. Imaging characteristics of the 3 cases of anti-PD-1 antibody-related pneumonitis

PATIENT 1	PATIENT 2	PATIENT 3
Baseline CT		
No interstitial lung abnormalities	Centrilobular emphysema and RB-ILD* in upper lungs	No interstitial lung abnormalities
CT during therapy prior to diagnosis of pneumonitis		
2 weeks prior: Peripheral consolidations, GGO, and reticular opacities in lower lungs (Fig.A)	***3 weeks prior:*** No change since baseline, no finding suggestive of drug-related pneumonitis	No CT between baseline and dx of pneumonitis
CT at clinical diagnosis of pneumonitis		
Findings: - Diffuse **GGO** - Diffuse **reticular opacities** - Lower lobe **consolidations** - **Traction bronchiectasis** - **Decreased lung volumes** - **Pleural effusions** ***Extent:*** - All lobe involved • 25-50% in upper lungs • >50% in middle lungs • >50% in lower lungs (Fig.B)	***Findings:*** - Diffuse **GGO** - Diffuse **reticular opacities** - **Consolidations** - **Traction bronchiectasis** - **Centrilobular nodularity** - **Decreased lung volumes** ***Extent:*** - All lobes involved • >50% in upper lungs • >50% in middle lungs • >50% in lower lungs (Fig. C)	***Findings:*** - Peripheral and lower lung **GGO** - Peripheral and lower lung **reticular opacities** - Peripheral and lower lung **consolidations** ***Extent:*** - All lobes involved • 5-25% of upper lungs • 5-25% of middle lungs • 25-50% of lower lungs (Fig. D)
Radiological Follow-up		
Marked decrease of all findings at 2 wks and 10 wks after the onset	No follow-up CT scan	All findings decreased on 3 follow-up scans off therapy; No recurrent pneumonitis on follow-up scans over 39 months since restarting therapy
Classification		
AIP/ARDS	**AIP/ARDS**	**NSIP**

RB-ILD: respiratory bronchitis-interstitial lung disease, which is one of the manifestation of smoking related lung disease

GGOs: ground glass opacity

AIP: acute interstitial pneumonia

ARDS: acute respiratory distress syndrome

NSIP: non-specific interstitial pneumonia