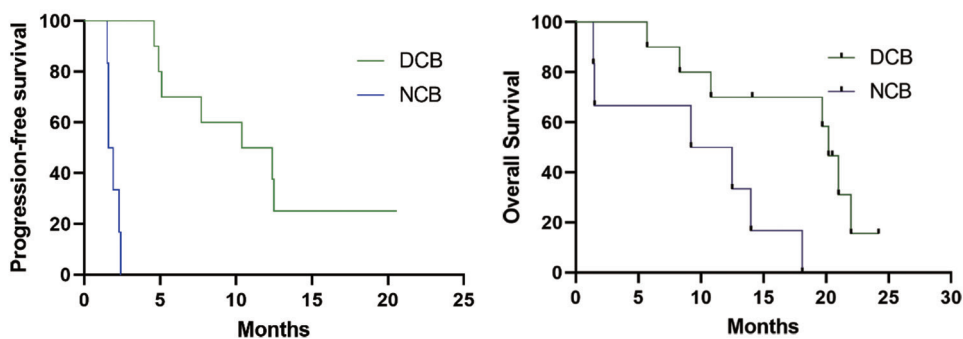
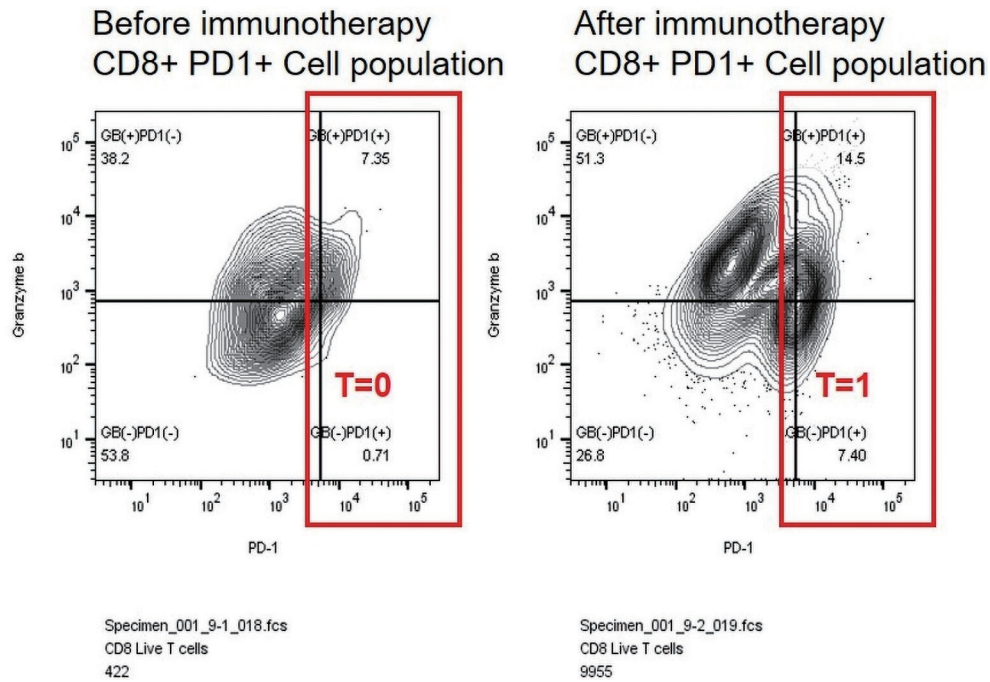


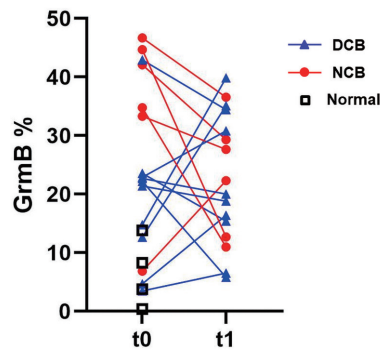
**Figure S1** Gating strategy for flow cytometric analysis. (A) Gating strategy for PD-1<sup>+</sup> CD8<sup>+</sup> T cells and (B) co-receptor expression. PD-1, programmed cell death-1; GB, granzyme B; SSC-A, Side Scatter Area; FSC-A, forward scatter area; 7aad, 7-amino actinomycin D.



**Figure S2** Progression-free survival and overall survival of NSCLC patients. The median PFS of DCB was 11.40 months, and that of NCB was 1.75 months ( $P < 0.0001$ ). The median OS of DCB was 28.20 months, and that of NCB was 10.85 months. The hazard ratio (95% confidence interval of ratio) for OS was 0.16 (0.03-0.84) for patients regardless of PD-L1 TPS expression. The survival curves are significantly different with  $P = 0.013$ . DCB, durable clinical benefit; NCB, no clinical benefit.



**Figure S3** Representative images of FACS analysis on peripheral blood mononuclear cells (PBMCs) from patients before and after treatment with immune check point inhibitors. Flow cytometry images of the PD-1<sup>+</sup>CD8<sup>+</sup> T-cell population. PD-1, programmed cell death-1; GB, granzyme B.



**Figure S4** Proliferative response of PD-1<sup>+</sup>CD8<sup>+</sup> T cells containing GrmB in peripheral blood collected before (t0) and after anti-PD-1 therapy (t1). Changes in percentage of PD-1<sup>+</sup>CD8<sup>+</sup> T cells containing GrmB from patients with normal patients (n=4) and lung cancer (n=16) before and after immune check point inhibitors. DCB, durable clinical benefit; NCB, no clinical benefit; GrmB, granzyme B; t0, before immunotherapy; t1, after immunotherapy.

**Table S1** Patient's clinicopathological characteristics

Patient ID	Age/Sex	Histology	Smoking status	TNM stage	PD-L1 <sup>a</sup>	ICI	Time to sampling (days)	Response
1	77/M	SQC	Ex-smoker	IV	2	Nivo	21	PD
2	68/M	SQC	Current smoker	IV	2	Nivo	18	PD
3	71/M	SQC	Current smoker	IV	1	Nivo	18	SD
4	50/M	SQC	Current smoker	IV	1	Nivo	17	SD
5	68/M	SQC	Current smoker	IV	2	Pembro	21	SD
6	85/M	SQC	Ex-smoker	IIIc	2	Pembro	21	SD
7	81/M	SQC	Ex-smoker	IV	2	Pembro	22	PR
8	61/M	ADC	Ex-smoker	IV	2	Pembro	21	PR
9	46/M	ADC	Current smoker	IV	1	Nivo	18	PD
10	75/M	ADC	Current smoker	IV	2	Atezo	21	PD
11	58/M	SQC	Ex-smoker	IV	0	Pembro	21	PD
12	79/M	SQC	Ex-smoker	IIIc	2	Atezo	21	SD <sup>b</sup>
13	79/M	ADC	Current smoker	IV	2	Pembro	20	SD
14	73/M	SQC	Current smoker	IV	0	Atezo	25	SD
15	67/M	ADC	Ex-smoker	IV	1	Atezo	25	SD
16	87/M	ADC	Ex-smoker	IIIc	0	Atezo	21	PD

<sup>a</sup> PD-L1 expression (SP263, TPS): 0%: 0 vs. 1-49%: 1 vs. ≥50%: 2. SQC: squamous cell carcinoma; ADC: adenocarcinoma; PD: progressive disease; SD: stable disease; PR: partial response; ICI: immune checkpoint inhibitors; Nivo: nivolumab; Pembro: pembrolizumab; Atezo: atezolizumab.

**Table S2** Antibody information

Antibody	Source	Catalog No
Anti-Mouse CD8a (Clone: 5.3-6.7)	Biolegend	100710
Anti-Human/Mouse Granzyme B (Clone: QA16A02)	Biolegend	372214
Anti-Mouse CD279 (PD-1) (Clone: J43)	eBiosciences	12-9985-82
Anti-Human FoxP3 (Clone: PCH101)	eBiosciences	11-4776-42
Anti-Human CD152 (CTLA-4) (Clone: L3D10)	Biolegend	349908
Anti-Human CD223 (LAG-3) (Clone: 3DS223H)	eBiosciences	56-2239-42
Anti-Human CD336 (Tim-3) (Clone: F38-2E2)	Biolegend	345026
7-AAD staining solution	Abcam	ab228563