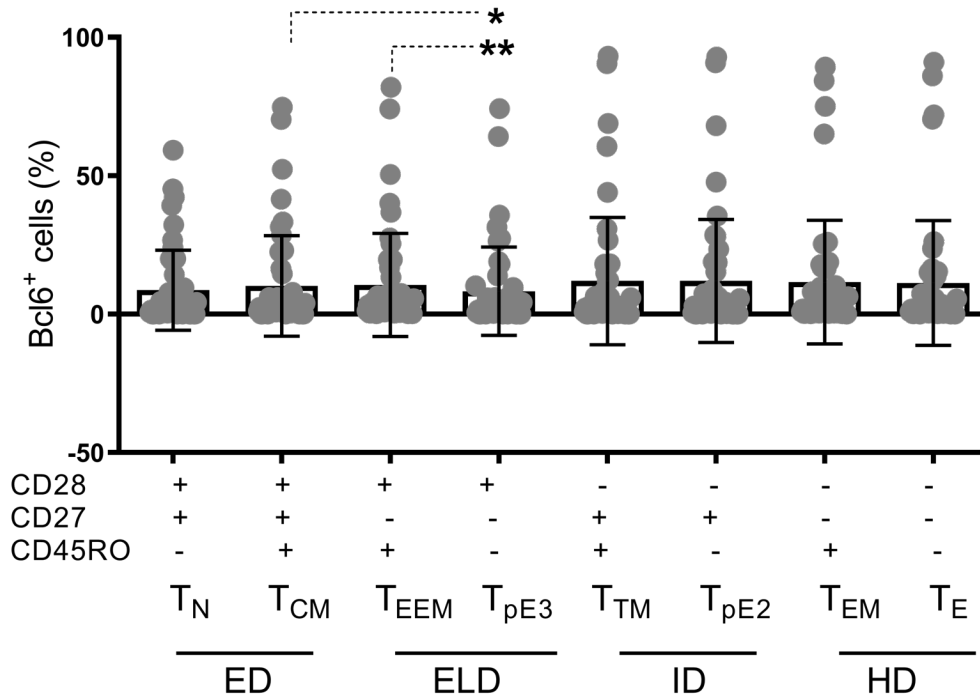
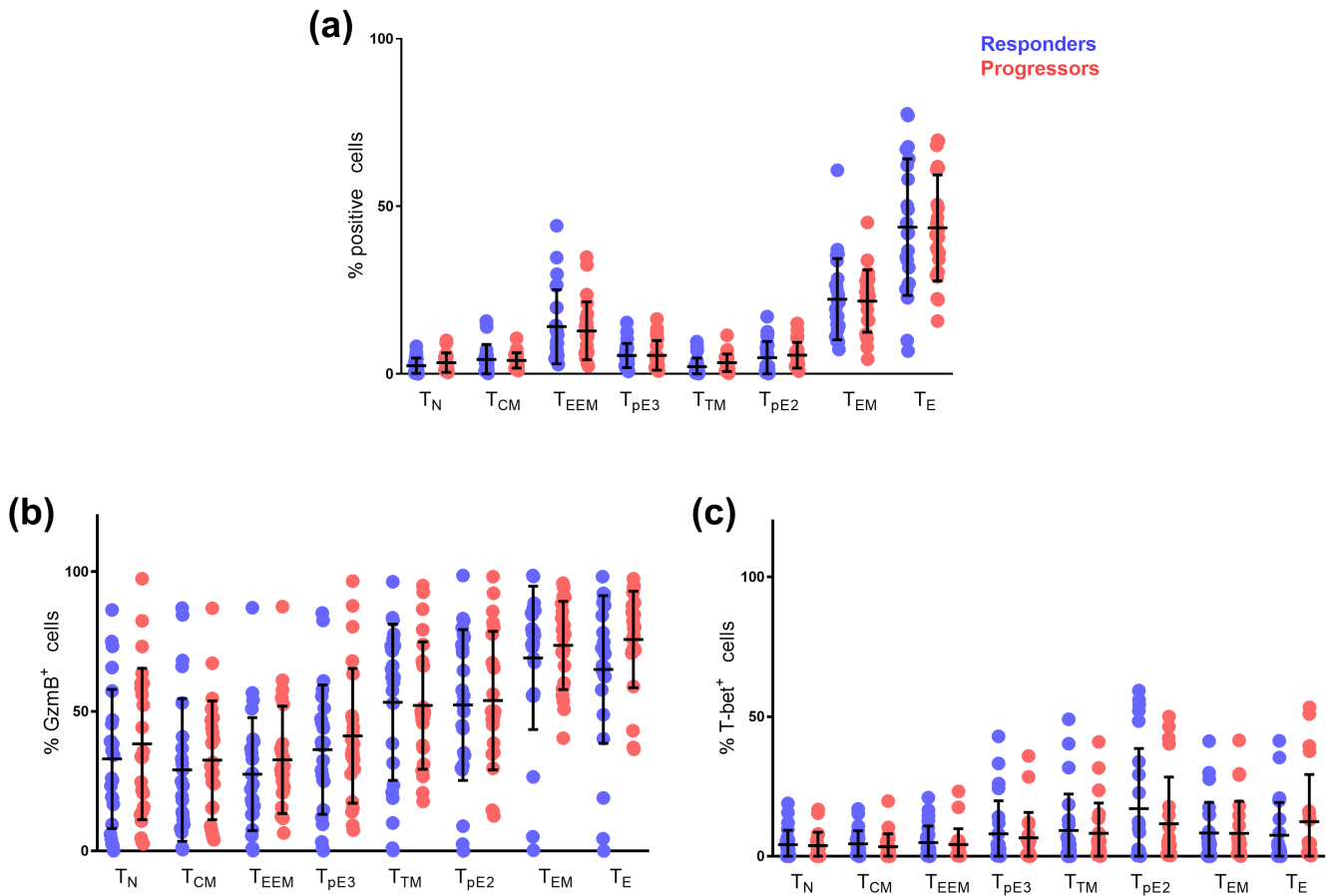


**Supporting Information**

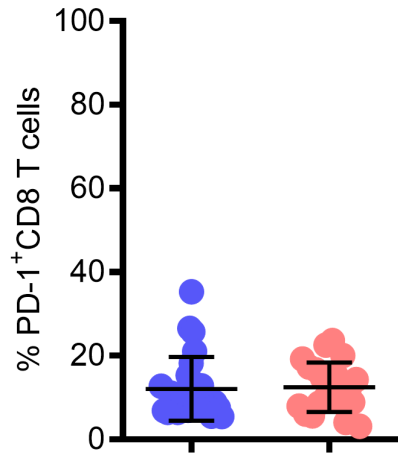


**Supplementary figure 1.** Frequencies of BCL-6<sup>+</sup> cells in CD8<sup>+</sup> T cell differentiation subsets at baseline. ED, early differentiated state; ELD, early like differentiated state; ID, intermediate differentiated state; HD, highly differentiated state. \*  $P < 0.05$ , \*\*  $P < 0.01$ .

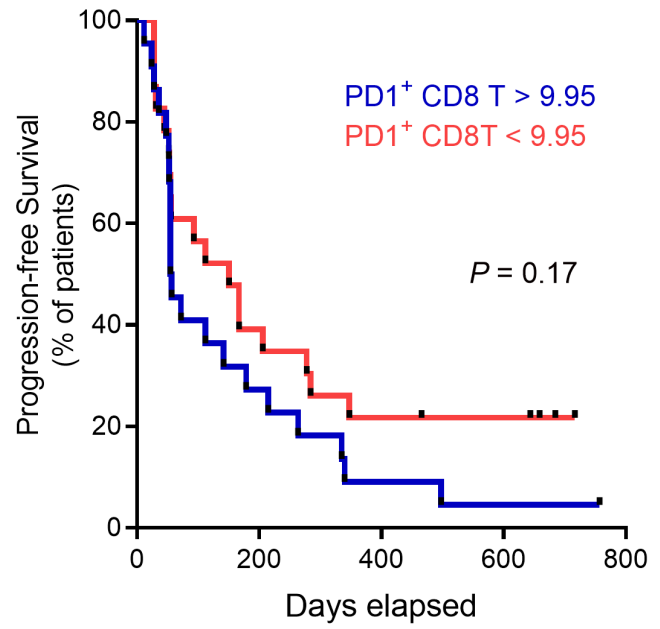


**Supplementary figure 2.** (a) Comparison of the frequencies of CD8<sup>+</sup> T cell differentiation subsets at baseline between responders (blue circles) and progressors (red circles) of NSCLC patients receiving nivolumab therapy. Comparison of the frequencies of GzmB<sup>+</sup> (b) and T-bet<sup>+</sup> (c) in CD8<sup>+</sup> T cell differentiation subsets at the baseline between responders (blue circles) and progressors (red circles) of NSCLC patients receiving nivolumab therapy.

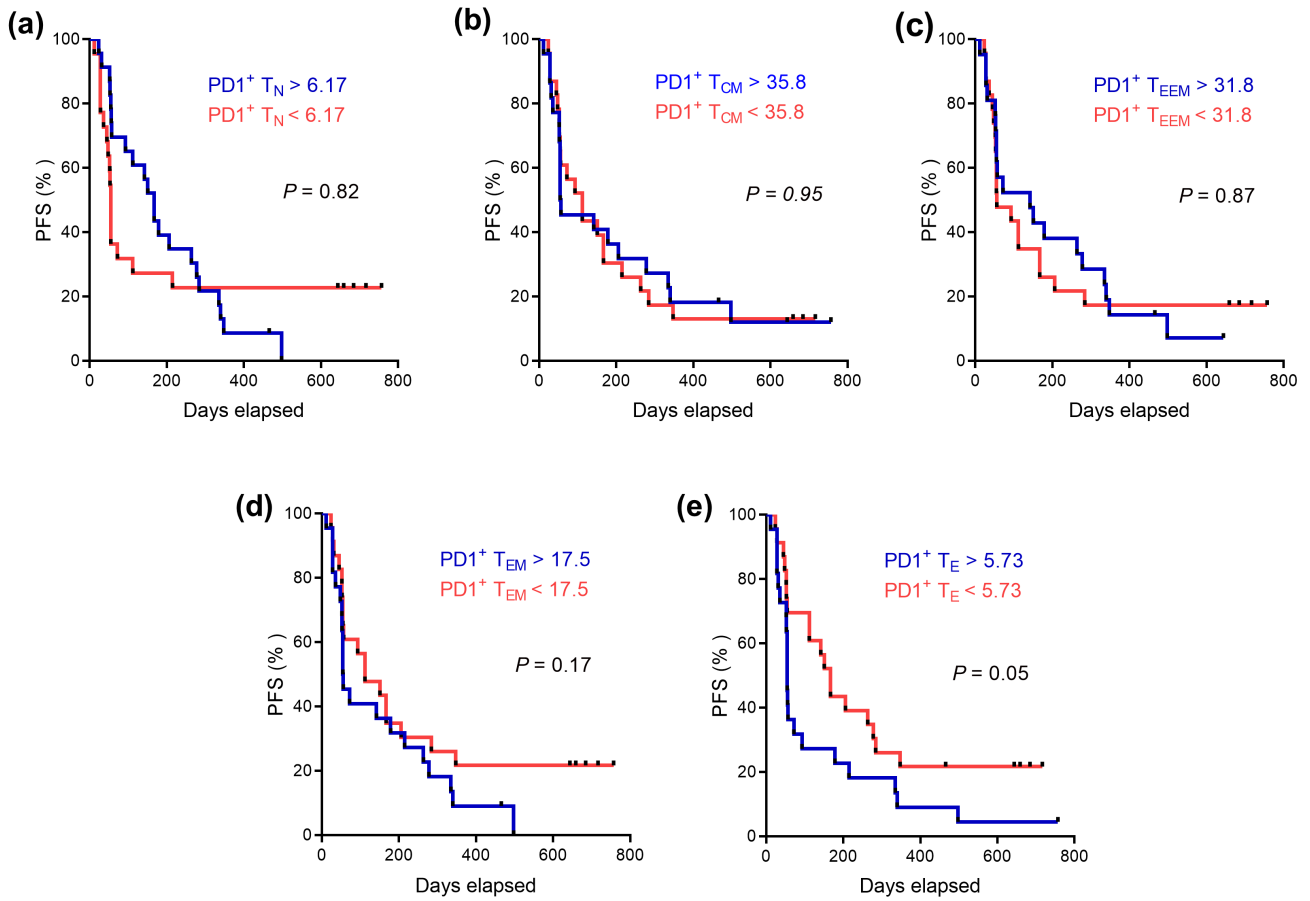
**(a)**



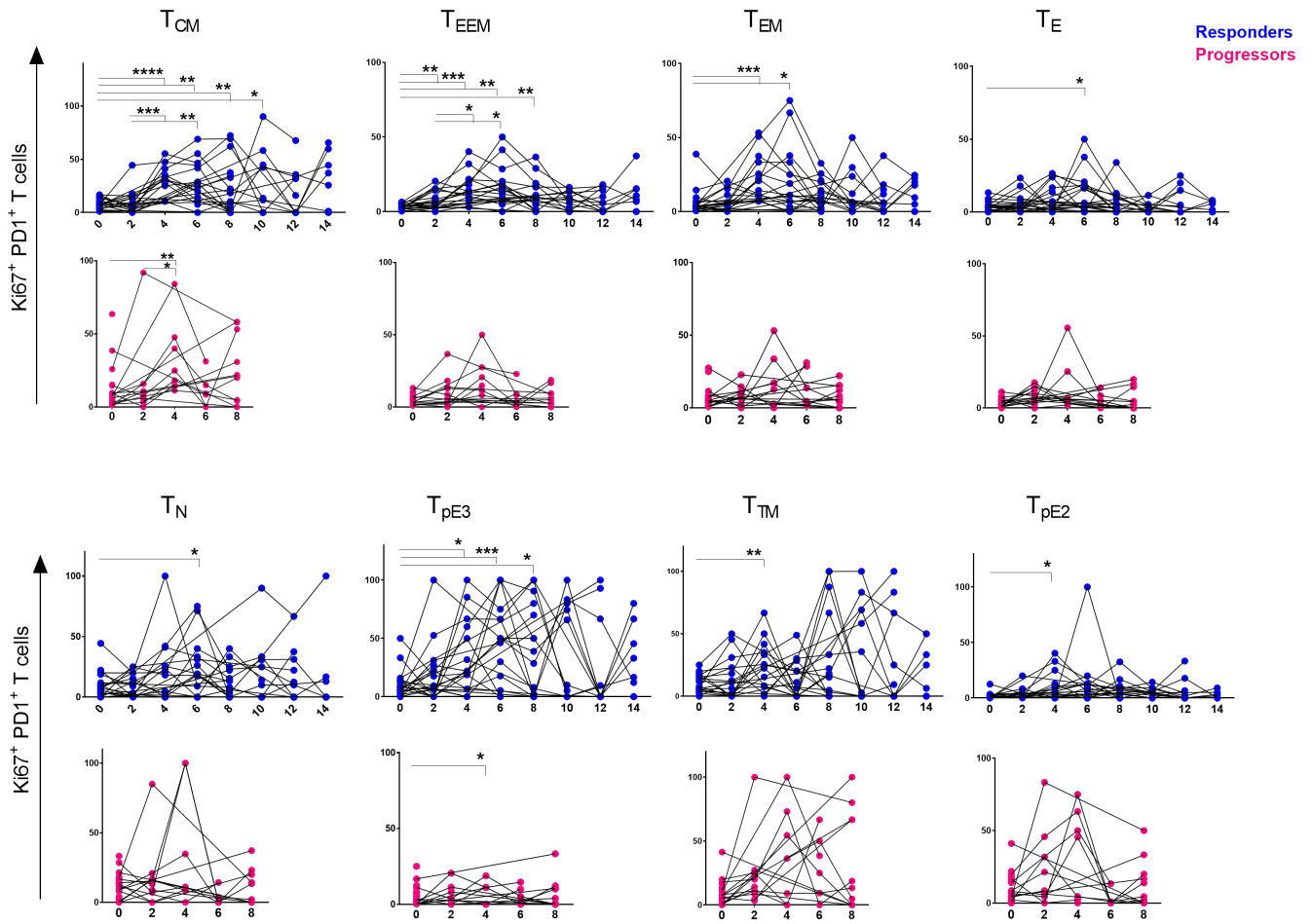
**(b)**



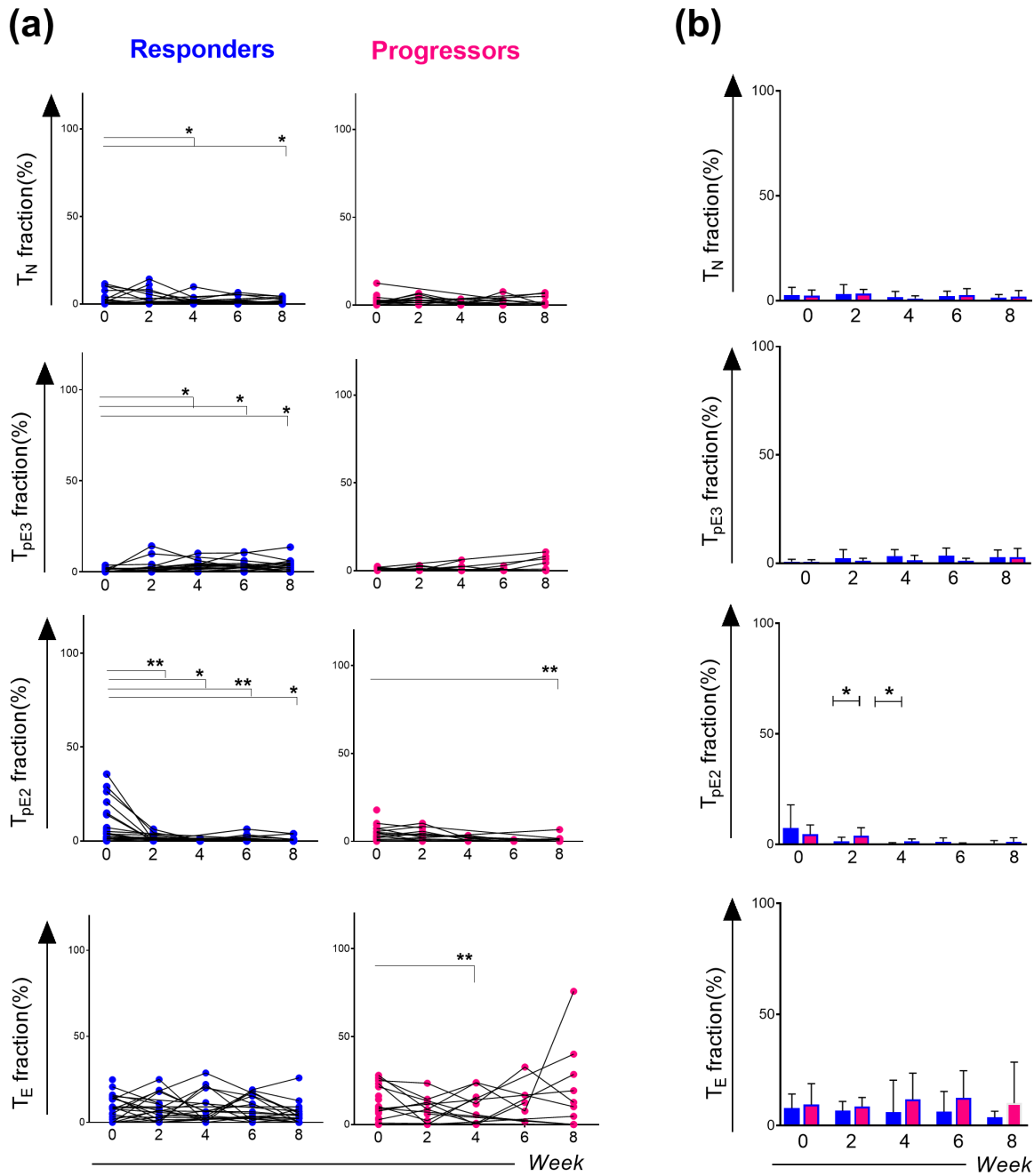
**Supplementary figure 3. (a)** Frequencies of PD-1 positive cells in total CD8<sup>+</sup> T cell population in responders (blue dots) and progressors (red dots) at baseline. **(b)** Kaplan–Meier PFS curves of baseline frequencies of PD-1<sup>+</sup>CD8<sup>+</sup> T cells.



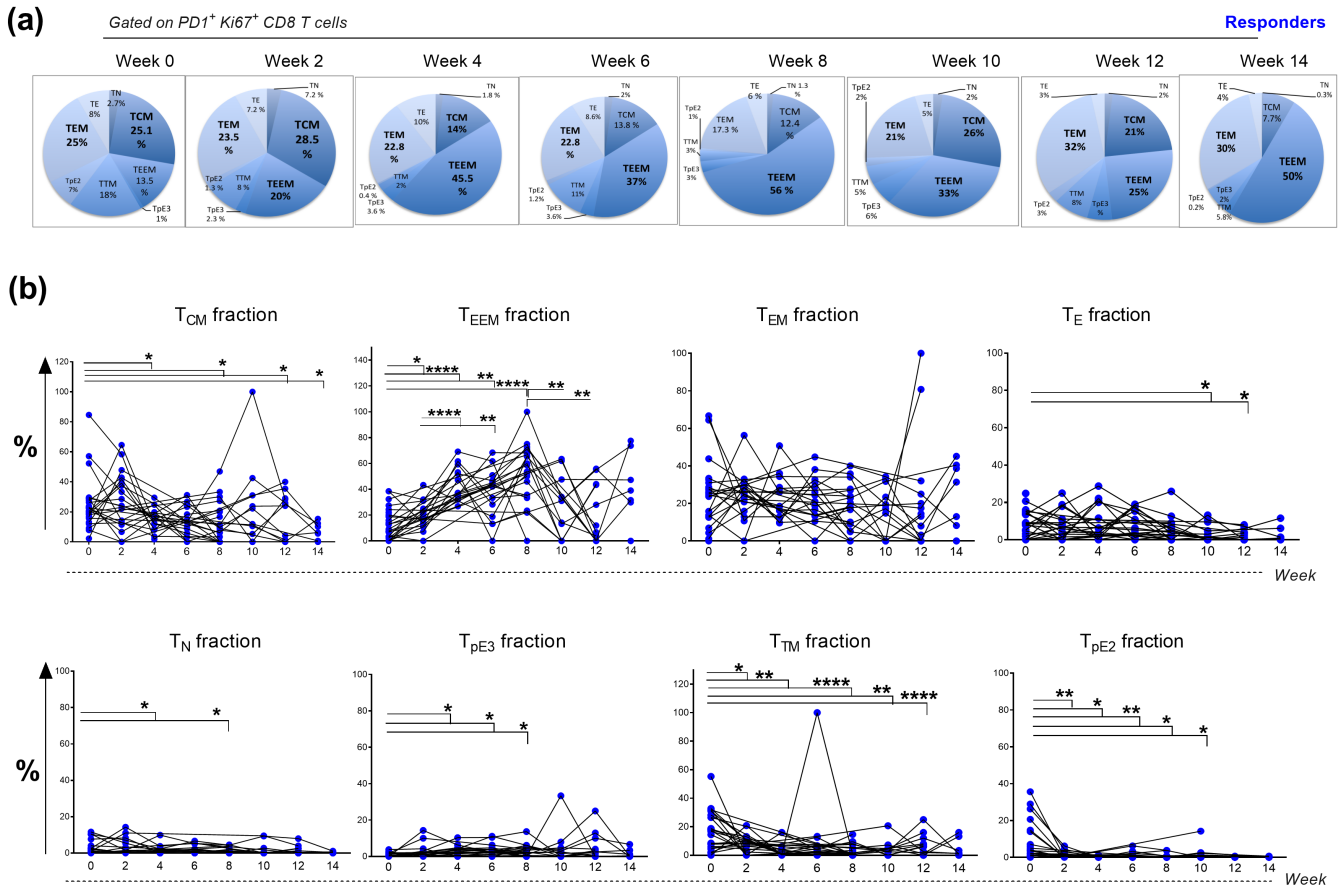
**Supplementary figure 4.** Kaplan–Meier PFS curves of peripheral PD-1<sup>+</sup>CD8<sup>+</sup>T<sub>N</sub> (a), PD-1<sup>+</sup>CD8<sup>+</sup>T<sub>CM</sub> (b), PD-1<sup>+</sup>CD8<sup>+</sup>T<sub>EEM</sub> (c), PD-1<sup>+</sup>CD8<sup>+</sup>T<sub>EM</sub> (d), PD-1<sup>+</sup>CD8<sup>+</sup>T<sub>E</sub> and (e) cell percentages at baseline.



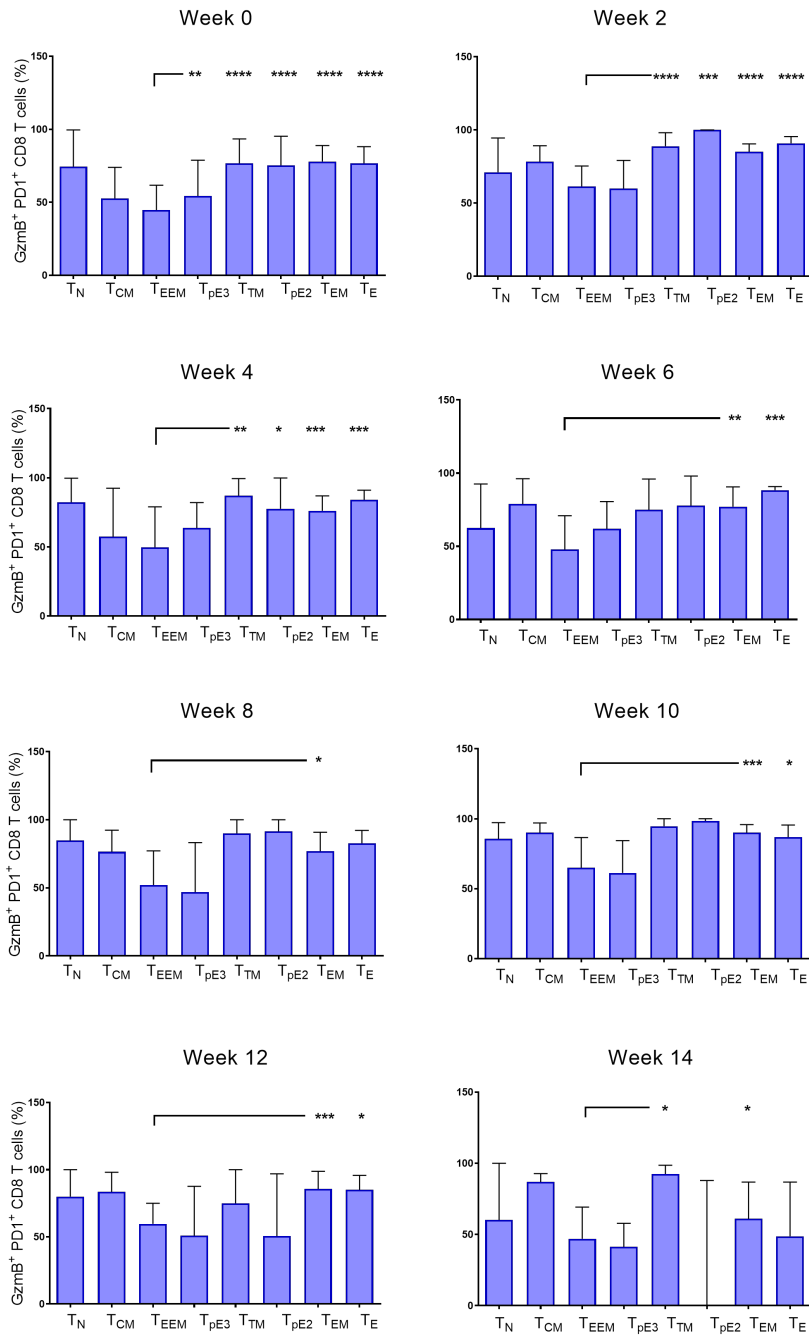
**Supplementary figure 5.** Extended kinetics of proliferating PD-1<sup>+</sup> subsets upon several time points of PD-1 blockade in the discovery cohort: Graphs showing the kinetics of cycling Ki67<sup>+</sup>PD-1<sup>+</sup>CD8<sup>+</sup> T subsets upon multiple cycle of nivolumab therapy (0, 2, 4, 6, 8, 10, 12 and 14 weeks) in responders (n = 17) (blue dots) and progressors (n = 10) (red dots). Data were analyzed using the Wilcoxon matched-pairs signed-rank test.



**Supplementary figure 6. (a)** Kinetics of  $T_N$ ,  $T_{pE2}$ ,  $T_{pE3}$  and  $T_E$  fractions in  $PD-1^+Ki67^+CD8^+$  T cells at week 0, 2, 4, 6 and week 8 in responders (blue dots) and progressors (red dots). **(b)** Comparison of  $PD1^+ Ki67^+$  cells from  $CD8^+$   $T_N$ ,  $T_{pE2}$ ,  $T_{pE3}$  and  $T_E$  T cell differentiation subsets between responders (blue dots) and progressors (red dots) at different time points. \*  $P < 0.05$ , \*\*  $P < 0.01$ .



**Supplementary figure 7. (a)** Subset fractions of Ki67<sup>+</sup>PD-1<sup>+</sup>CD8<sup>+</sup> T cells from week 0 to week 14 in responders of NSCLC patients receiving nivolumab monotherapy. **(b)** Graphs showing kinetics of cycling Ki67<sup>+</sup>PD-1<sup>+</sup>CD8<sup>+</sup> T cell subsets at different time points in the responder group after therapy. \*  $P < 0.05$ , \*\*  $P < 0.01$ , \*\*\*  $P < 0.001$ , \*\*\*\*  $P < 0.0001$ .



**Supplementary figure 8.** Frequencies of granzyme B positive cells in each PD1<sup>+</sup>CD8<sup>+</sup> T cell subset at the baseline (week0) and at different time points after nivolumab therapy (week 2, 4, 6, 8, 10, 12 and 14) in responders. Data were analyzed with the Wilcoxon matched-pairs signed-rank test. \*  $P < 0.05$ , \*\*  $P < 0.01$ , \*\*\*  $P < 0.001$ , \*\*\*\*  $P < 0.0001$ .



**Supplementary table 1.** Extended clinical characteristics of responder patients from both discovery and validation cohorts.

	Discovery Cohort Responders (Nivolumab, Checkmate 870) (n=24)				Validation Cohort Responders Anti-PD1 immunotherapy (n=18)		
Responders	PFS (Days)	PD status	Response	Responders	PFS (Days)	PD status	Response
R1	466	0	PR	R1	98	1	SD
R2	151	1	PR	R2	202	1	SD
R3	167	1	SD	R3	315	1	SD
R4	717	0	SD	R4	202	1	SD
R5	264	1	SD	R5	257	1	SD
R6	340	1	SD	R6	729	1	PR
R7	112	1	SD	R7	436	0	PR
R8	757	0	SD	R8	99	1	SD
R9	644	0	PR	R9	373	0	SD
R10	206	1	SD	R10	182	1	SD
R11	142	1	SD	R11	350	1	SD
R12	685	0	SD	R12	126	1	SD
R13	72	1	SD	R13	115	1	SD
R14	335	1	SD	R14	112	1	SD
R15	179	1	SD	R15	447	1	SD
R16	112	1	SD	R16	432	0	PR
R17	93	1	SD	R17	238	1	SD
R18	167	1	SD	R18	425	0	SD
R19	659	0	PR				
R20	284	1	SD				
R21	348	1	PR				
R22	215	1	SD				
R23	498	1	PR				
R24	278	1	PR				

**PFS**, Progress Free Survival; **PD**, Progressive disease (0: no progression, 1: already progressed); **PR**, Partial Response; **SD**, Stable Disease.