Supplementary

Table S1 Comparative analysis of CTC counts based on response to immune checkpoint inhibitor treatment

CTC count per 7.5 mL of blood in each cycle	NDB	DCB	P-value
C1 *vs.* C2			
C1 < C2 (n=33)	23 (66)	10 (44)	0.081
C1 > C2 (n=25)	12 (34)	13 (57)	
C1 *vs.* C3			
C1 < C3 (n=14)	8 (44)	6 (26)	0.219
C1 > C3 (n=27)	10 (56)	17 (74)	
C1 *vs.* C4			
C1 < C4 (n=11)	4 (80)	7 (32)	0.071
C1 > C4 (n=16)	1 (20)	15 (68)	
C2 *vs.* C3			
C2 < C3 (n=11)	6 (32)	5 (28)	0.800
C2 > C3 (n=26)	13 (68)	13 (72)	
C2 *vs.* C4			
C2 < C4 (n=11)	5 (83)	6 (35)	0.059
C2 > C4 (n=12)	1 (17)	11 (65)	
C3 *vs.* C4			
C3 < C4 (n=6)	2 (40)	4 (25)	0.450
C3 > C4 (n=15)	3 (60)	12 (75)	

Values are presented as number (%). NDB, non-durable benefit; DCB, durable clinical benefit; C1, cycle one C2, Cycle two.; CTC, circulating tumor cell.

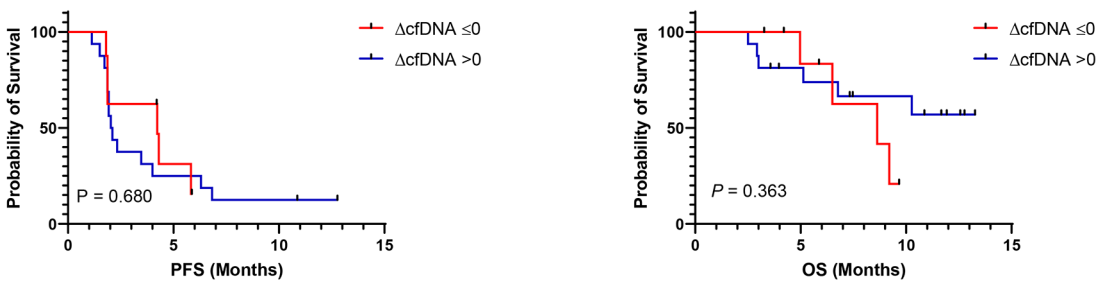

Figure S1 Survival analysis based on cfDNA levels during ICI treatment. PFS and OS analyses based on relative changes in the cfDNA levels from C1 to C4 (ΔcfDNA). cfDNA, circulating cell-free DNA; ICI, immune checkpoint inhibitor; PFS, progression-free survival; OS, overall survival; C1, cycle one; C2, cycle 2.

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Table S2 Univariate and multivariate analyses of PFS and OS

Variables	Univariate HR for PFS	95% CI	P-value	Multivariate HR for PFS	95% CI	P-value	Univariate HR for OS	95% CI	P-value	Multivariate HR for OS	95% CI	P-value
Age	0.97	0.95–1.00	0.072	-	-	-	1.02	0.98–1.06	0.292	-	-	-
Sex: Male (*vs.* Female)	0.62	0.36–1.06	0.081	0.30	0.12–0.74	0.009	0.68	0.35–1.32	0.255	0.37	0.13–1.01	0.051
Smoking (*vs.* Never smoker, n=17)												
Current smoker (n=29)	0.44	0.23–0.84	0.013	-	-	-	0.82	0.37–1.81	0.621	-	-	-
Ex-smoker (n=37)	0.53	0.29–0.98	0.044	-	-	-	0.65	0.29–1.43	0.281	-	-	-
EGFR mutation (*vs.* Activating mutation, n=16)												
Wild-type (n=50)	0.43	0.23–0.80	0.007	0.43	0.18–1.03	0.059	0.85	0.36–1.97	0.696	-	-	-
PD-L1 IHC TPS (*vs.* <50%)												
22C3: ≥50% (n=28)	0.44	0.24–0.80	0.007	-	-	-	0.60	0.29–1.24	0.167	-	-	-
SP263: ≥50% (n=20)	0.38	0.20–0.73	0.004	-	-	-	0.63	0.29–1.39	0.255	-	-	-
CTC count (*vs.* C1 < C2)												
C1>C2 (n=25)	0.59	0.33–1.08	0.086	0.33	0.14–0.78	0.012	0.37	0.16–0.89	0.027	0.27	0.08–0.93	0.038
Baseline (C1) NLR (*vs.* >4.0)												
≤4.0 (n=49)	0.59	0.36–0.98	0.042	-	-	-	0.52	0.28–0.99	0.048	-	-	-
Baseline (C1) dNLR (*vs.* >2.0)												
≤2.0 (n=42)	0.54	0.33–0.89	0.016	0.41	0.18–0.92	0.031	0.38	0.20–0.74	0.004	0.25	0.07–0.92	0.038
Baseline (C1) PLR (*vs.* >210)												
≤210 (n=42)	0.53	0.32–0.87	0.012	-	-	-	0.41	0.22–0.80	0.008	-	-	-
Baseline (C1) cfDNA (*vs.* >5.8)												
≤5.8 (n=9)	0.43	0.15–1.21	0.110	-	-	-	0.11	0.01–0.89	0.039	-	-	-

PFS, progression-free survival; CI, confidence interval; OS, overall survival; EGFR, epidermal growth factor receptor; IHC, immunohistochemistry; TPS, tumor proportional score; CTC, circulating tumor cell; NLR, neutrophil-to-lymphocyte ratio, dNLR, derived neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; cfDNA, circulating cell-free DNA; HR, hazard ratio; C1, cycle one; C2, cycle 2.

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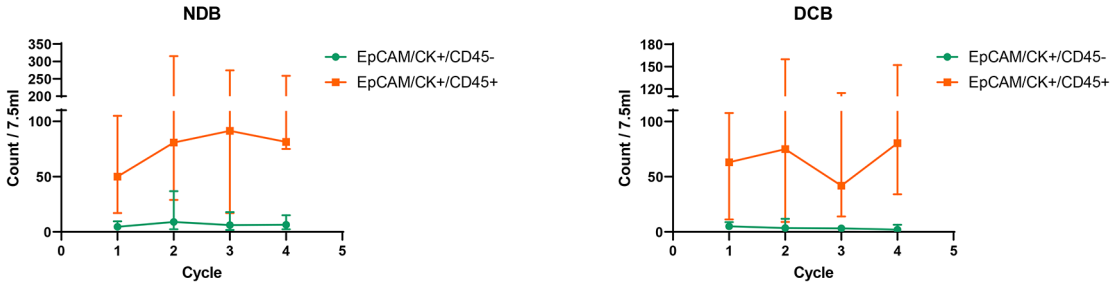

Figure S2 Dynamic changes in counts of CTCs (EpCAM/CK+/CD45–) and triple-positive cells (EpCAM/CK+/CD45+) during ICI treatment. CTC, circulating tumor cell; EpCAM, epithelial cell adhesion molecule; CK, cytokeratin; ICI, immune checkpoint inhibitor; NDB, non-durable benefit; DCB, durable clinical benefit.

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