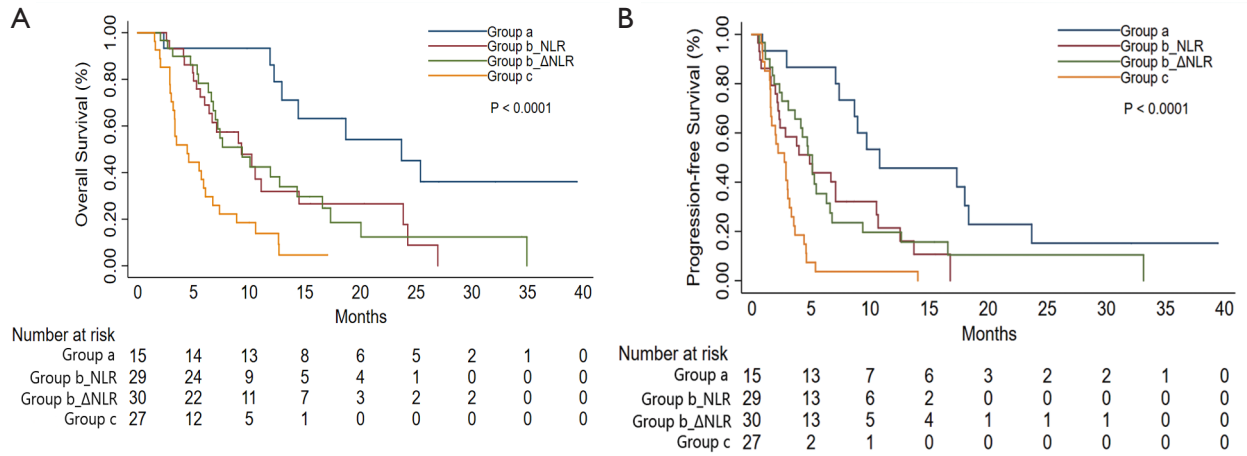


**Figure S1** Time-dependent receiver-operating curve of baseline neutrophil-to-lymphocyte ratio for overall survival. AUC, area under the curve.



**Figure S2** Kaplan-Meier curves of overall survival and progression-free survival for patients stratified by baseline neutrophil-to-lymphocyte ratio (NLR) and 6 weeks post-treatment NLR minus baseline NLR ( $\Delta$ NLR). (A) Overall survival; (B) progression-free survival.

**Table S1** Univariate analyses of factors associated with overall survival and progression-free survival

Characteristics	Overall survival		Progression-free survival	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (years)	1.00 (0.97–1.01)	0.223	0.99 (0.97–1.00)	0.070
Age ≥65 years	0.74 (0.47–1.17)	0.194	0.59 (0.38–0.90)	0.015*
Sex (male)	0.99 (0.60–1.64)	0.977	0.86 (0.54–1.37)	0.528
ECOG PS 3–4	1.12 (0.70–1.81)	0.632	1.05 (0.67–1.63)	0.835
Smoker status (current or former smoker)	0.85 (0.54–1.34)	0.482	0.89 (0.58–1.36)	0.583
Histology				
Squamous	1 (ref)		1 (ref)	
Adenocarcinoma	0.88 (0.53–1.46)	0.620	0.89 (0.55–1.43)	0.631
Others	0.92 (0.34–2.45)	0.860	0.88 (0.33–2.34)	0.795
Stage IV	2.32 (0.98–5.50)	0.056	1.91 (0.91–4.02)	0.090
Prior chemotherapy (yes)	1.45 (0.88–2.38)	0.146	1.73 (1.10–2.73)	0.018*
Prior target therapy (yes)	1.24 (0.79–1.97)	0.352	1.75 (1.14–2.70)	0.011*
Prior thoracic radiotherapy (yes)	0.94 (0.52–1.68)	0.830	1.50 (0.88–2.57)	0.135
Positive EGFR mutation (yes)	1.34 (0.78–2.32)	0.295	1.71 (1.02–2.88)	0.043*
Positive ALK translocation (yes)	0.55 (0.08–4.02)	0.556	0.31 (0.04–2.28)	0.249
PD-L1 expression				
<1	1 (ref)		1 (ref)	
1–49	2.03 (0.86–4.82)	0.107	1.37 (0.66–2.86)	0.398
≥50	0.88 (0.32–2.37)	0.795	0.72 (0.33–1.59)	0.417
Not examined	1.63 (0.80–3.34)	0.183	1.02 (0.56–1.85)	0.961
Combined with other therapy (yes)	0.79 (0.50–1.24)	0.307	0.94 (0.61–1.43)	0.755
Antibiotics received within 1 month before (yes)	1.27 (0.79–2.03)	0.318	1.64 (1.06–2.53)	0.025*
Immunotherapy as systemic				
1	1 (ref)		1 (ref)	
2	1.30 (0.69–2.43)	0.420	1.62 (0.91–2.87)	0.100
≥3	1.57 (0.87–2.86)	0.136	2.08 (1.20–3.60)	0.009*
PD-1 inhibition agent				
Nivolumab	1 (ref)		1 (ref)	
Pembrolizumab	1.38 (0.87–2.20)	0.173	1.23 (0.78–1.92)	0.373
others	0.26 (0.04–1.93)	0.189	0.59 (0.18–1.90)	0.374
NLR ≥4.5	2.28 (1.41–3.67)	<0.001*	2.21 (1.41–3.48)	<0.001*
ΔNLR ≥0	2.11 (1.31–3.38)	0.002*	1.94 (1.25–3.01)	0.003*

\*, P<0.05 indicates statistical significance. ALK, anaplastic lymphoma kinase; CI, confidence interval; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EGFR, epidermal growth factor receptor; HR, hazards ratio; NLR, neutrophil-to-lymphocyte ratio; PD-1, programmed cell death 1; ref, reference category; ΔNLR, 6 weeks post-treatment NLR minus baseline NLR.

**Table S2** Multivariate analysis of the associations of NLR and  $\Delta$ NLR with survival

Characteristics	Overall survival		Progression-free survival	
	HR (95% CI)	P value	HR (95% CI)	P value
Age $\geq$ 65 years	0.84 (0.46–1.54)	0.580	0.59 (0.33–1.05)	0.072
Prior chemotherapy (yes)	2.06 (0.96–4.43)	0.063	2.72 (1.37–5.40)	0.004*
Prior target therapy (yes)	1.10 (0.56–2.17)	0.791	1.73 (0.94–3.20)	0.080
Positive EGFR mutation (yes)	1.33 (0.63–2.78)	0.452	1.22 (0.61–2.44)	0.574
Antibiotics received within 1 month before	1.00 (0.61–1.66)	0.989	1.44 (0.90–2.31)	0.125
Immunotherapy as systemic				
1	1 (ref)		1 (ref)	
2	0.77 (0.32–1.89)	0.571	0.68 (0.31–1.48)	0.392
$\geq$ 3	0.48 (0.15–1.52)	0.212	0.37 (0.13–1.05)	0.061
Group a	1 (ref)		1 (ref)	
Group b	3.12 (1.35–7.21)	0.008*	3.45 (1.62–7.36)	0.001*
Group c	10.79 (4.30–27.10)	<0.0001*	10.49 (4.39–25.09)	<0.0001*

\*,  $P < 0.05$  indicates statistical significance. CI, confidence interval; EGFR, epidermal growth factor receptor; HR, hazards ratio; NLR, neutrophil-to-lymphocyte ratio; ref, reference category;  $\Delta$ NLR, 6 weeks post-treatment NLR minus baseline NLR.