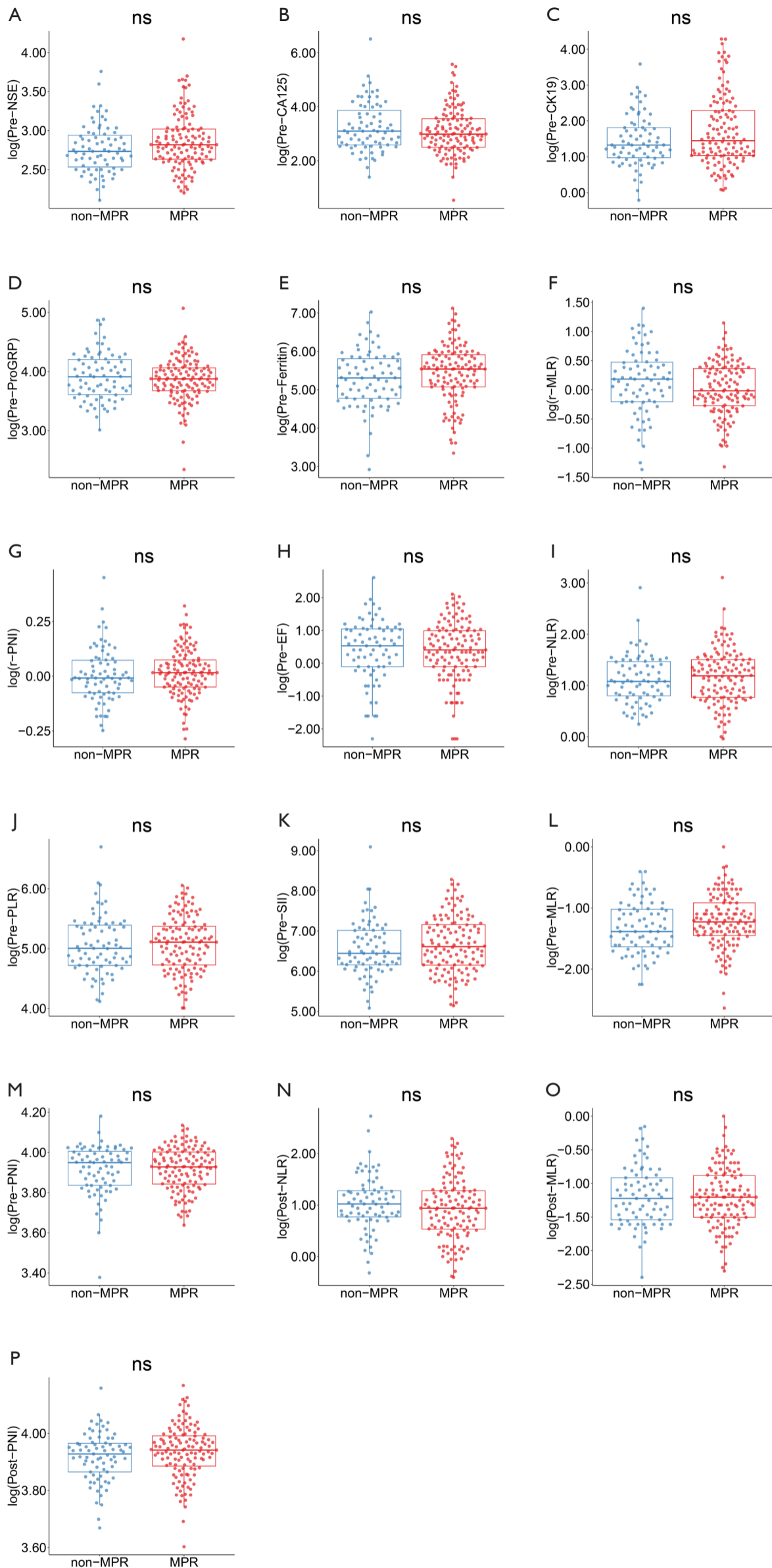**Table S1** Immunotherapy regimen for patients included in the study

Therapy regimen	Number of patients (N=199)
Sugemalimab	2
Durvalumab	8
Sintilimab	11
Serplulimab	11
Nivolumab	15
Camrelizumab	15
Toripalimab	24
Pembrolizumab	33
Tislelizumab	80

Table S2 Comparison of median values of blood biomarkers between the MPR and non-MPR groups

Variables	Median		P value
	Non-MPR	MPR	
Pre-NSE	15.4	16.7	0.09
Pre-CA125	22.2	19.9	0.32
Pre-CEA	3.0	2.1	0.01
Pre-CK19	3.8	4.3	0.15
Pre-ProGRP	49.9	48.2	0.64
Pre-SCCA	1.0	1.4	0.01
Pre-ferritin	202.1	255.0	0.11
r-EF	0.5	0.7	0.03
r-NLR	1.0	0.8	0.047
r-PLR	0.9	0.7	0.004
r-SII	0.9	0.5	0.004
r-MLR	1.2	1.0	0.09
r-PNI	1.0	1.0	0.22
Pre-EF	1.7	1.5	0.77
Pre-NLR	2.9	3.3	0.42
Pre-PLR	149.2	165.0	0.63
Pre-SII	629.4	743.0	0.27
Pre-MLR	0.3	0.3	0.07
Pre-PNI	51.9	50.8	0.91
Post-EF	0.9	1.4	0.03
Post-NLR	2.8	2.6	0.17
Post-PLR	148.2	116.0	0.009
Post-SII	526.1	416.0	0.01
Post-MLR	0.3	0.3	0.95
Post-PNI	50.8	51.5	0.16

MPR, major pathological response; NSE, neuron-specific enolase; CA125, carbohydrate antigen 125; CEA, carcinoembryonic antigen; CK19, cytokeratin 19; ProGRP, progastrin-releasing peptide; SCCA, squamous cell carcinoma antigen; r, relative; EF, eosinophil fraction; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; SII, systemic immune-inflammation index; MLR, monocyte-to-lymphocyte ratio; PNI, prognostic nutritional index.
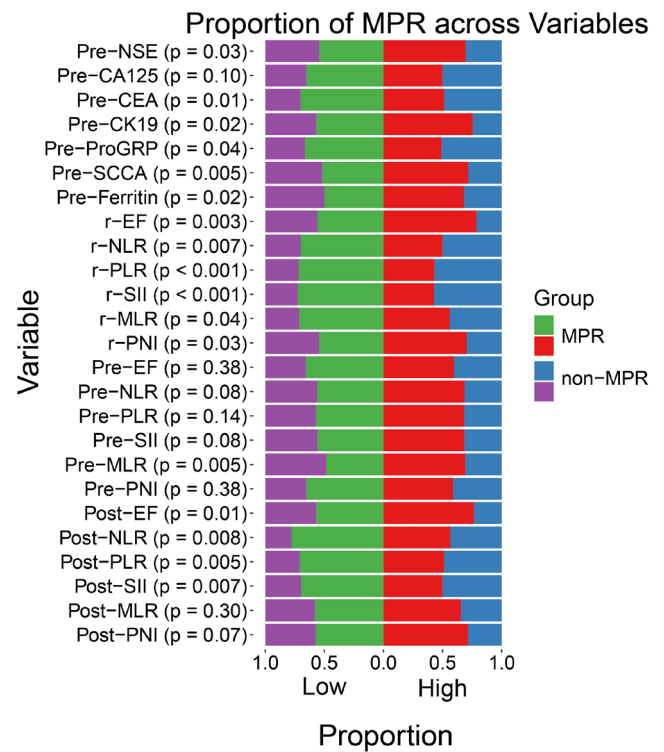
Figure S1 Distribution characteristics of serum tumor markers (A-E) and peripheral blood inflammation-based biomarkers (F-P) in the MPR group and the non-MPR group. ns, not significant. MPR, major pathological response; NSE, neuron-specific enolase; CA125, carbohydrate antigen 125; ProGRP, progastrin-releasing peptide; MLR, monocyte-to-lymphocyte ratio; PNI, prognostic nutritional index; EF, eosinophil fraction; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; SII, systemic immune-inflammation index.

Table S3 Optimal cut-off value of serum tumor markers and peripheral blood biomarkers for predicting MPR in the neoadjuvant chemo-immunotherapy cohort

Variables	Cut-off values	AUC	Sensitivity	Specificity
Pre-NSE	15.97	0.57	0.59	0.57
Pre-CA125	53.84	0.54	0.85	0.25
Pre-CEA	2.75	0.61	0.66	0.53
Pre-CK19	7.43	0.56	0.35	0.81
Pre-ProGRP	62.00	0.52	0.81	0.32
Pre-SCCA	1.15	0.61	0.61	0.60
Pre-ferritin	159.95	0.57	0.75	0.41
r-EF	1.38	0.59	0.35	0.84
r-NLR	0.95	0.58	0.69	0.51
r-PLR	0.95	0.62	0.77	0.49
r-SII	0.83	0.62	0.77	0.52
r-MLR	0.94	0.57	0.48	0.68
r-PNI	1.01	0.55	0.56	0.61
Pre-EF	1.45	0.51	0.49	0.57
Pre-NLR	3.11	0.53	0.56	0.57
Pre-PLR	163.61	0.52	0.52	0.60
Pre-SII	661.38	0.55	0.57	0.56
Pre-MLR	0.24	0.58	0.74	0.45
Pre-PNI	51.95	0.50	0.57	0.49
Post-EF	2.35	0.59	0.34	0.83
Post-NLR	1.95	0.56	0.34	0.84
Post-PLR	140.28	0.61	0.65	0.56
Post-SII	530.68	0.60	0.70	0.49
Post-MLR	0.26	0.50	0.64	0.44
Post-PNI	52.55	0.56	0.40	0.73

MPR, major pathological response; AUC, area under curve; NSE, neuron-specific enolase; CA125, carbohydrate antigen 125; CEA, carcinoembryonic antigen; CK19, cytokeratin 19; ProGRP, progastrin-releasing peptide; SCCA, squamous cell carcinoma antigen; r, relative; EF, eosinophil fraction; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; SII, systemic immune-inflammation index; MLR, monocyte-to-lymphocyte ratio; PNI, prognostic nutritional index.

Figure S2 MPR rate across blood biomarkers. MPR, major pathological response; NSE, neuron-specific enolase; CA125, carbohydrate antigen 125; CEA, carcinoembryonic antigen; CK19, cytokeratin 19; ProGRP, progastrin-releasing peptide; SCCA, squamous cell carcinoma antigen; r, relative; EF, eosinophil fraction; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; SII, systemic immune-inflammation index; MLR, monocyte-to-lymphocyte ratio; PNI, prognostic nutritional index.

Table S4 Univariate regression analysis of MPR

Variables	Univariate	
	OR (95% CI)	P value
Gender: male (*vs.* female)	8.79 (2.83–27.31)	<0.001
Age: ≥65 years (*vs.* <65 years)	1.52 (0.85–2.71)	0.16
Smoking history: ever (*vs.* never)	3.84 (2.02–7.29)	<0.001
BMI: under/overweight (*vs.* normal weight)	0.74 (0.38–1.41)	0.35
Clinical stage: III (*vs.* I/II)	1.56 (0.87–2.81)	0.14
Tumor location: LUL/RLL/RML/RUL (*vs.* LLL)	1.20 (0.49–2.93)	0.69
	0.91 (0.37–2.25)	0.84
	2.60 (0.26–25.93)	0.42
	1.09 (0.46–2.62)	0.84
Pre-CT tumor size: ≤50 mm (*vs.* >50 mm)	0.43 (0.23–0.80)	0.01
Histological type: LUSC (*vs.* LUAD)	5.44 (2.77–10.67)	<0.001
Pre-NSE: low (*vs.* high)	0.52 (0.29–0.93)	0.03
Pre-CA125: low (*vs.* high)	1.87 (0.92–3.83)	0.08
Pre-CEA: low (*vs.* high)	2.23 (1.24–4.01)	0.01
Pre-CK19: low (*vs.* high)	0.43 (0.22–0.86)	0.02
Pre-ProGRP: low (*vs.* high)	2.07 (1.06–4.01)	0.03
Pre-SCCA: low (*vs.* high)	0.42 (0.23–0.76)	0.004
Pre-ferritin: low (*vs.* high)	0.47 (0.26–0.87)	0.02
r-EF: low (*vs.* high)	0.35 (0.17–0.71)	0.004
r-NLR: low (*vs.* high)	2.32 (1.29–4.20)	0.005
r-PLR: low (*vs.* high)	3.34 (1.80–6.19)	<0.001
r-SII: low (*vs.* high)	3.55 (1.92–6.56)	<0.001
r-MLR: low (*vs.* high)	1.93 (1.06–3.51)	0.03
r-PNI: low (*vs.* high)	0.50 (0.28–0.90)	0.02
Pre-EF: low (*vs.* high)	1.30 (0.73–2.32)	0.37
Pre-NLR: low (*vs.* high)	0.59 (0.33–1.06)	0.08
Pre-PLR: low (*vs.* high)	0.63 (0.35–1.12)	0.11
Pre-SII: low (*vs.* high)	0.59 (0.33–1.05)	0.07
Pre-MLR: low (*vs.* high)	0.42 (0.23–0.77)	0.005
Pre-PNI: low (*vs.* high)	1.30 (0.73–2.32)	0.37
Post-EF: low (*vs.* high)	0.41 (0.20–0.83)	0.01
Post-NLR: low (*vs.* high)	2.69 (1.31–5.53)	0.007
Post-PLR: low (*vs.* high)	2.31 (1.29–4.16)	0.005
Post-SII: low (*vs.* high)	2.29 (1.26–4.15)	0.006
Post-MLR: low (*vs.* high)	0.72 (0.40–1.30)	0.28
Post-PNI: low (*vs.* high)	0.54 (0.29–1.01)	0.05

MPR, major pathological response; OR, odds ratio; CI, confidence interval; BMI, body mass index; LUL, left upper lung; RLL, right lower lung; RML, right middle lung; RUL, right upper lung; LLL, left lower lung; CT, computed tomography; LUSC, lung squamous cell carcinoma; LUAD, lung adenocarcinoma; NSE, neuron-specific enolase; CA125, carbohydrate antigen 125; CEA, carcinoembryonic antigen; CK19, cytokeratin 19; ProGRP, progastrin-releasing peptide; SCCA, squamous cell carcinoma antigen; r, relative; EF, eosinophil fraction; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; SII, systemic immune-inflammation index; MLR, monocyte-to-lymphocyte ratio; PNI, prognostic nutritional index.

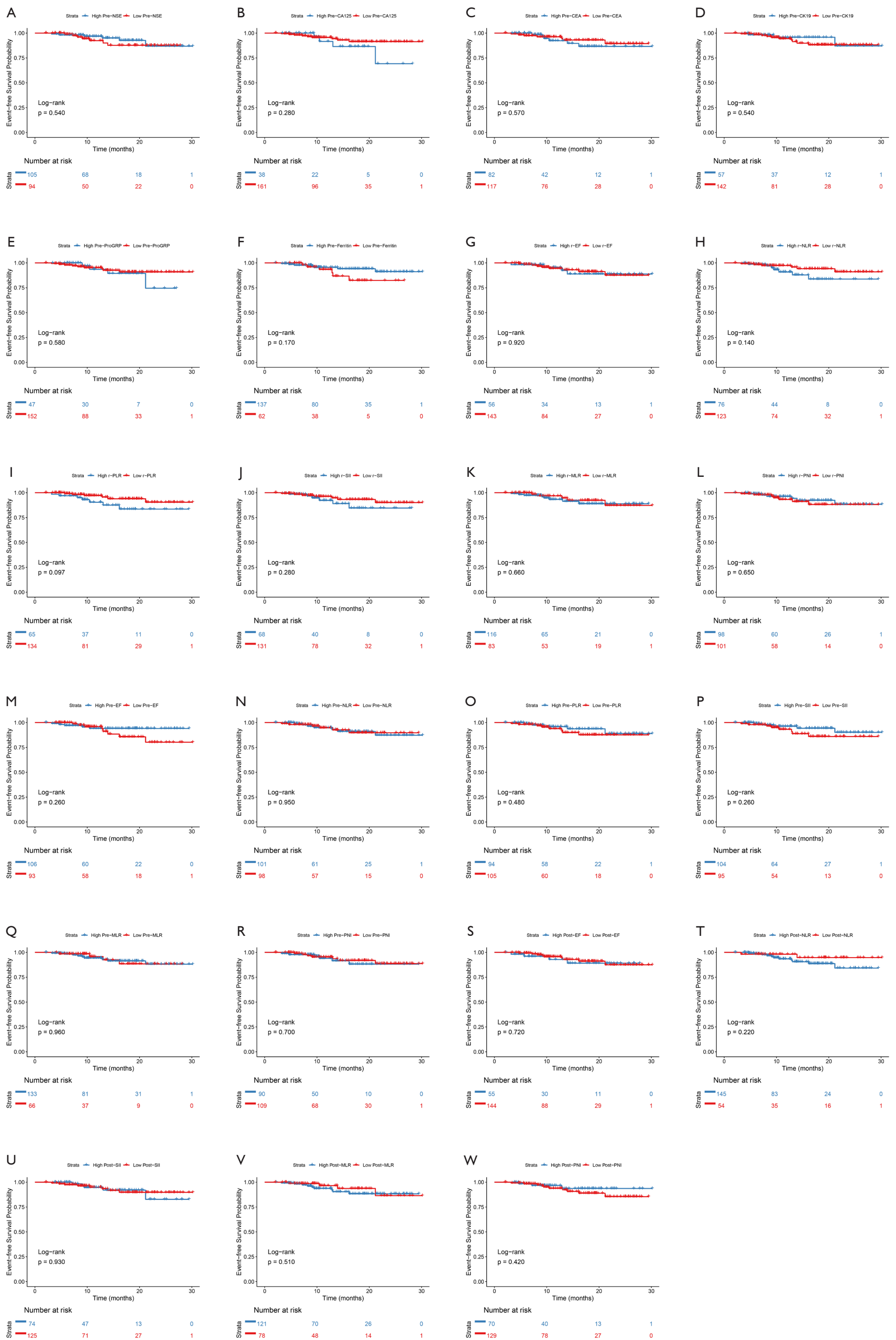**Table S5** Multivariable regression analysis of MPR

Variables	Multivariable	
	OR (95% CI)	P value
Gender: male (*vs.* female)	0.91 (0.16–5.05)	0.91
Smoking history: ever (*vs.* never)	3.47 (1.34–8.95)	0.01
Pre-CT tumor size: ≤50 mm (*vs.* >50 mm)	0.73 (0.26–2.04)	0.55
Histological type: LUSC (*vs.* LUAD)	2.33 (0.83–6.52)	0.11
Pre-NSE: low (*vs.* high)	0.44 (0.20–0.95)	0.04
Pre-CEA: low (*vs.* high)	2.20 (0.95–5.08)	0.07
Pre-CK19: low (*vs.* high)	0.79 (0.25–2.52)	0.69
Pre-ProGRP: low (*vs.* high)	1.32 (0.55–3.15)	0.53
Pre-SCCA: low (*vs.* high)	0.74 (0.32–1.75)	0.50
Pre-ferritin: low (*vs.* high)	1.15 (0.49–2.70)	0.75
r-EF: low (*vs.* high)	0.51 (0.19–1.41)	0.20
r-NLR: low (*vs.* high)	0.79 (0.24–2.61)	0.70
r-PLR: low (*vs.* high)	1.87 (0.68–5.13)	0.22
r-SII: low (*vs.* high)	1.70 (0.50–5.73)	0.40
r-MLR: low (*vs.* high)	0.61 (0.25–1.48)	0.28
r-PNI: low (*vs.* high)	0.96 (0.43–2.14)	0.91
Pre-MLR: low (*vs.* high)	0.73 (0.28–1.95)	0.53
Post-EF: low (*vs.* high)	0.49 (0.18–1.32)	0.16
Post-NLR: low (*vs.* high)	2.87 (1.00–8.24)	0.051
Post-PLR: low (*vs.* high)	1.40 (0.55–3.55)	0.48
Post-SII: low (*vs.* high)	1.39 (0.51–3.77)	0.52

MPR, major pathological response; OR, odds ratio; CI, confidence interval; CT, computed tomography; LUSC, lung squamous cell carcinoma; LUAD, lung adenocarcinoma; NSE, neuron-specific enolase; CEA, carcinoembryonic antigen; CK19, cytokeratin 19; ProGRP, progastrin-releasing peptide; SCCA, squamous cell carcinoma antigen; r, relative; EF, eosinophil fraction; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; SII, systemic immune-inflammation index; MLR, monocyte-to-lymphocyte ratio; PNI, prognostic nutritional index.
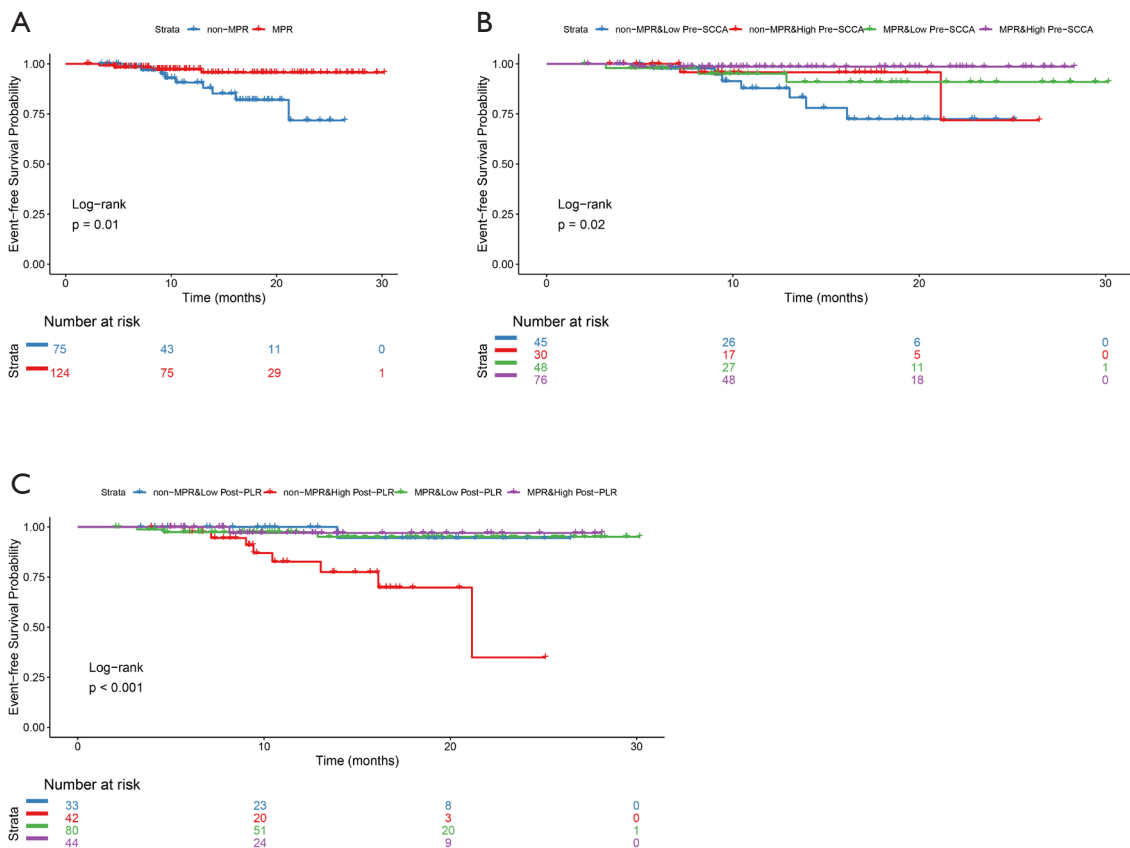
Table S6 Multicollinearity diagnosis based on multivariate regression analysis of MPR

Variables	VIF	Collinear statistical tolerance
Gender	2.002	0.500
Smoking history	1.566	0.639
Pre-CT tumor size	1.874	0.534
Histological type	1.740	0.575
Pre-NSE	1.211	0.826
Pre-CEA	1.411	0.709
Pre-CK19	2.016	0.496
Pre-ProGRP	1.133	0.882
Pre-SCCA	1.487	0.672
Pre-ferritin	1.322	0.756
r-EF	1.380	0.724
r-NLR	2.868	0.349
r-PLR	1.870	0.535
r-SII	2.855	0.350
r-MLR	1.513	0.661
r-PNI	1.308	0.765
Pre-MLR	1.688	0.592
Post-EF	1.392	0.718
Post-NLR	1.511	0.662
Post-PLR	1.740	0.575
Post-SII	1.948	0.513

MPR, major pathological response; VIF, variance inflation factor; CT, computed tomography; NSE, neuron-specific enolase; CEA, carcinoembryonic antigen; CK19, cytokeratin 19; ProGRP, progastrin-releasing peptide; SCCA, squamous cell carcinoma antigen; r, relative; EF, eosinophil fraction; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; SII, systemic immune-inflammation index; MLR, monocyte-to-lymphocyte ratio; PNI, prognostic nutritional index.

Figure S3 The relationship between serum tumor markers (A-F) and peripheral blood inflammation-based biomarkers (G-W) and patient EFS. EFS, event-free survival; NSE, neuron-specific enolase; CA125, carbohydrate antigen 125; CEA, carcinoembryonic antigen; CK19, cytokeratin 19; ProGRP, progastrin-releasing peptide; EF, eosinophil fraction; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; SII, systemic immune-inflammation index; MLR, monocyte-to-lymphocyte ratio; PNI, prognostic nutritional index.

Figure S4 KM survival analysis and log-rank tests of EFS between the MPR and non-MPR groups (A), and among the high and low pre-treatment SCCA level (B) and the post-treatment PLR (C) subgroups within these groups. MPR, major pathological response; SCCA, squamous cell carcinoma antigen; KM, Kaplan-Meier; EFS, event-free survival; PLR, platelet-lymphocyte ratio.

Table S7 Baseline characteristics of NSCLC patients in the control group receiving surgery alone

Variables	Subtypes	N=129, n (%)
Gender	Female	38 (29.5)
	Male	91 (70.5)
Age (years)	<65	81 (62.8)
	≥65	48 (37.2)
Smoking history	Never smoker	52 (40.3)
	Smoker or ex-smoker	77 (59.7)
BMI	Normal weight	96 (74.4)
	Under/overweight	33 (25.6)
Pre-CT tumor size	>30	64 (49.6)
	≤30	65 (50.4)
Clinical stage	I	95 (73.6)
	II	23 (17.8)
	III	11 (8.5)
Tumor location	LLL	30 (23.3)
	LUL	19 (14.7)
	RLL	29 (22.5)
	RML	12 (9.3)
	RUL	39 (30.2)
Histological type	LUAD	59 (45.7)
	LUSC	70 (54.3)

NSCLC, non-small cell lung cancer; BMI, body mass index; CT, computed tomography; LLL, left lower lung; LUL, left upper lung; RLL, right lower lung; RML, right middle lung; RUL, right upper lung; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma.

Table S8 Univariate and multivariate Cox analyses of OS in NSCLC patients undergoing surgery alone

Variables	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
Gender: male (*vs.* female)	3.45 (1.35–8.80)	0.01	0.37 (0.04–3.29)	0.38
Age: ≥65 years (*vs.* <65 years)	2.74 (1.49–5.05)	0.001	2.56 (1.36–4.80)	0.003
Smoking history: ever (*vs.* never)	4.38 (1.84–10.44)	0.001	2.98 (0.34–26.14)	0.33
BMI: under/overweight (*vs.* normal weight)	1.11 (0.56–2.23)	0.76	–	–
Clinical stage: III (*vs.* I/II)	3.48 (1.53–7.91)	0.003	1.63 (0.67–3.93)	0.28
Tumor location: LUL/RLL/RML/RUL (*vs.* LLL)	0.79 (0.30–2.09)	0.63	–	–
	1.14 (0.51–2.54)	0.75	–	–
	0.18 (0.02–1.36)	0.10	–	–
	0.56 (0.24–1.32)	0.19	–	–
Pre-CT tumor size: ≤30 mm (*vs.* >30 mm)	0.42 (0.22–0.81)	0.009	0.71 (0.34–1.49)	0.37
Histological type: LUSC (*vs.* LUAD)	4.33 (2.00–9.39)	<0.001	1.78 (0.57–5.53)	0.32
Pre-SCCA: low (*vs.* high)	0.30 (0.16–0.58)	<0.001	0.48 (0.23–0.99)	0.048

OS, overall survival; NSCLC, non-small cell lung cancer; HR, hazard ratio; CI, confidence interval; BMI, body mass index; LUL, left upper lung; RLL, right lower lung; RML, right middle lung; RUL, right upper lung; LLL, left lower lung; CT, computed tomography; LUSC, lung squamous cell carcinoma; LUAD, lung adenocarcinoma; SCCA, squamous cell carcinoma antigen.

Table S9 Univariate and multivariate Cox analyses of DFS in NSCLC patients undergoing surgery alone

Variables	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
Gender: male (*vs.* female)	2.45 (1.14–5.24)	0.02	1.02 (0.29–3.54)	0.98
Age: ≥65 years (*vs.* <65 years)	2.31 (1.32–4.05)	0.003	2.14 (1.20–3.81)	0.01
Smoking history: ever (*vs.* never)	2.28 (1.18–4.40)	0.01	1.18 (0.33–4.17)	0.80
BMI: under/overweight (*vs.* normal weight)	1.05 (0.54–2.01)	0.90	–	–
Clinical stage: III (*vs.* I/II)	0.55 (0.31–0.98)	0.04	1.63 (0.67–3.94)	0.28
Tumor location: LUL/RLL/RML/RUL (*vs.* LLL)	2.89 (1.28–6.50)	0.01	–	–
	0.95 (0.39–2.36)	0.92	–	–
	1.17 (0.54–2.54)	0.69	–	–
	0.36 (0.08–1.61)	0.18	–	–
Pre-CT tumor size: ≤30 mm (*vs.* >30 mm)	0.75 (0.34–1.62)	0.46	0.78 (0.40–1.51)	0.46
Histological type: LUSC (*vs.* LUAD)	2.21 (1.20–4.07)	0.01	1.11 (0.43–2.88)	0.82
Pre-SCCA: low (*vs.* high)	0.39 (0.22–0.71)	0.002	0.52 (0.27–0.99)	0.047

DFS, disease-free survival; NSCLC, non-small cell lung cancer; HR, hazard ratio; CI, confidence interval; BMI, body mass index; LLL, left lower lung; LUL, left upper lung; RLL, right lower lung; RML, right middle lung; RUL, right upper lung; CT, computed tomography; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; SCCA, squamous cell carcinoma antigen.