

Supplementary

Table S1 The factors associated with progression-free survival in extensive-stage small cell lung cancer with a P value ≥ 0.1 in the univariate analysis

Variables	Reference	HR (95% CI)	P value
Lymphocyte	–	0.71 (0.47, 1.08)	0.1108
ApoB_A_C	>0.89 vs. ≤ 0.89 g/L	0.68 (0.4, 1.17)	0.1646
TG_C	>1.26 vs. ≤ 1.26 mmol/L	1.31 (0.9, 1.91)	0.1651
CEA	–	1 (1, 1)	0.1657
KI_67	–	1.01 (1, 1.02)	0.1816
TC_C	>3.83 vs. ≤ 3.83 mmol/L	1.3 (0.88, 1.93)	0.19
Liver_M	Yes vs. no	1.28 (0.86, 1.9)	0.2265
Cytokeratin_C	>3.33 vs. ≤ 3.33 μ g/L	1.25 (0.85, 1.84)	0.2605
HDL_C	>0.86 vs. ≤ 0.86 mmol/L	1.32 (0.81, 2.15)	0.2666
CD56	Positive vs. negative	0.71 (0.39, 1.3)	0.2678
SEAA_C	>0.65 vs. ≤ 0.65 μ g/L	1.32 (0.79, 2.23)	0.2913
KI_67_C	>60% vs. $\leq 60\%$	1.26 (0.77, 2.08)	0.3563
PLT	–	1 (1, 1)	0.3606
Neutrophil_C	>4.1 vs. $\leq 4.1 \times 10^9$ /L	0.84 (0.58, 1.23)	0.3693
Neutrophil	–	0.96 (0.87, 1.05)	0.3745
Blood_sodium	–	0.98 (0.94, 1.03)	0.3907
NLR	–	1.05 (0.94, 1.17)	0.4033
Monocyte_C	>0.8 vs. $\leq 0.8 \times 10^9$ /L	0.81 (0.48, 1.38)	0.4407
Brain_M	Yes vs. no	1.19 (0.7, 2.04)	0.5135
TG	–	1.11 (0.78, 1.58)	0.5475
Gender	Male vs. female	1.28 (0.41, 4.05)	0.6707
TTF-1	Positive vs. negative	0.91 (0.56, 1.48)	0.698
TC	–	1.04 (0.84, 1.28)	0.7335
ApoB_A	–	0.88 (0.39, 1.96)	0.7469
Monocyte	–	1.02 (0.87, 1.21)	0.7836
SYN	Positive vs. negative	1.07 (0.52, 2.21)	0.8546
CEA_C	>21.5 vs. ≤ 21.5 μ g/L	1.05 (0.59, 1.87)	0.8774
Cytokeratin	–	1 (0.96, 1.05)	0.8827
FIB	–	1.01 (0.91, 1.12)	0.8886
CA19-9	–	1 (1, 1)	0.9116
SEAA	–	1.01 (0.9, 1.13)	0.9249
ApoB	–	1.05 (0.37, 2.97)	0.9292
CA19-9_C	>6.8 vs. ≤ 6.8 U/mL	0.97 (0.52, 1.82)	0.9314
HDL	–	0.97 (0.48, 1.98)	0.9381
Other_M	Yes vs. no	1.02 (0.6, 1.74)	0.9431
LDL	–	0.99 (0.74, 1.32)	0.9548
ApoA1	–	1.01 (0.46, 2.23)	0.979
Smoking	Yes vs. no	0.99 (0.62, 1.6)	0.9819

HR, hazard ratio; CI, confidence interval; ApoB_A, ApoB/ApoA1 ratio; ApoB, apolipoprotein B; ApoA1, apolipoprotein A1; C, denotes the clinical features converted to categorical variables; TG, triglyceride; CEA, carcinoembryonic antigen; TC, total cholesterol; M, metastasis; HDL, high-density lipoprotein; CD56, cluster of differentiation 56; SEAA, squamous epithelial associated antigen; PLT, platelet; NLR, neutrophil-to-lymphocyte ratio; TTF-1, thyroid transcription factor 1; SYN, synuclein; FIB, fibrinogen; CA19-9, cancer antigen 19-9; LDL, low-density lipoprotein.

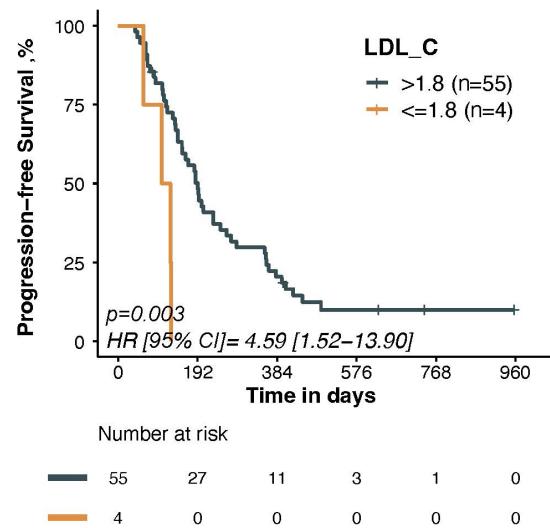


Figure S1 The Kaplan-Meier curve illustrates the PFS data for the two subgroups categorized by LDL levels of 1.8 mmol/L in the first-line immunochemotherapy cohort. LDL, low-density lipoprotein; HR, hazard ratio; CI, confidence interval; PFS, progression-free survival.

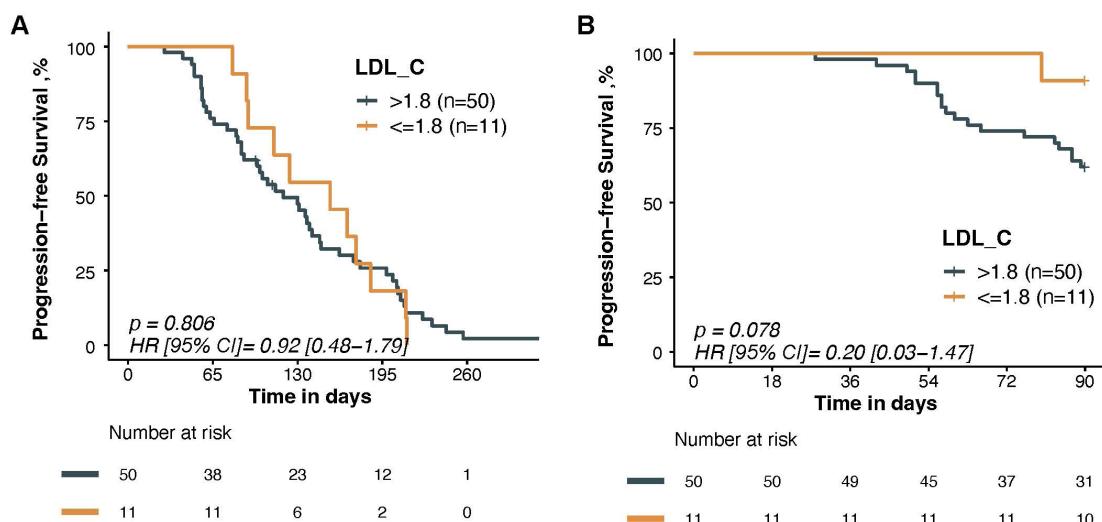


Figure S2 The Kaplan-Meier curve visualizes the PFS (A) and 3-month PFS (B) of the two patient subgroups categorized by LDL levels of 1.8 mmol/L in the first-line chemotherapy cohort. LDL, low-density lipoprotein; HR, hazard ratio; CI, confidence interval; PFS, progression-free survival.

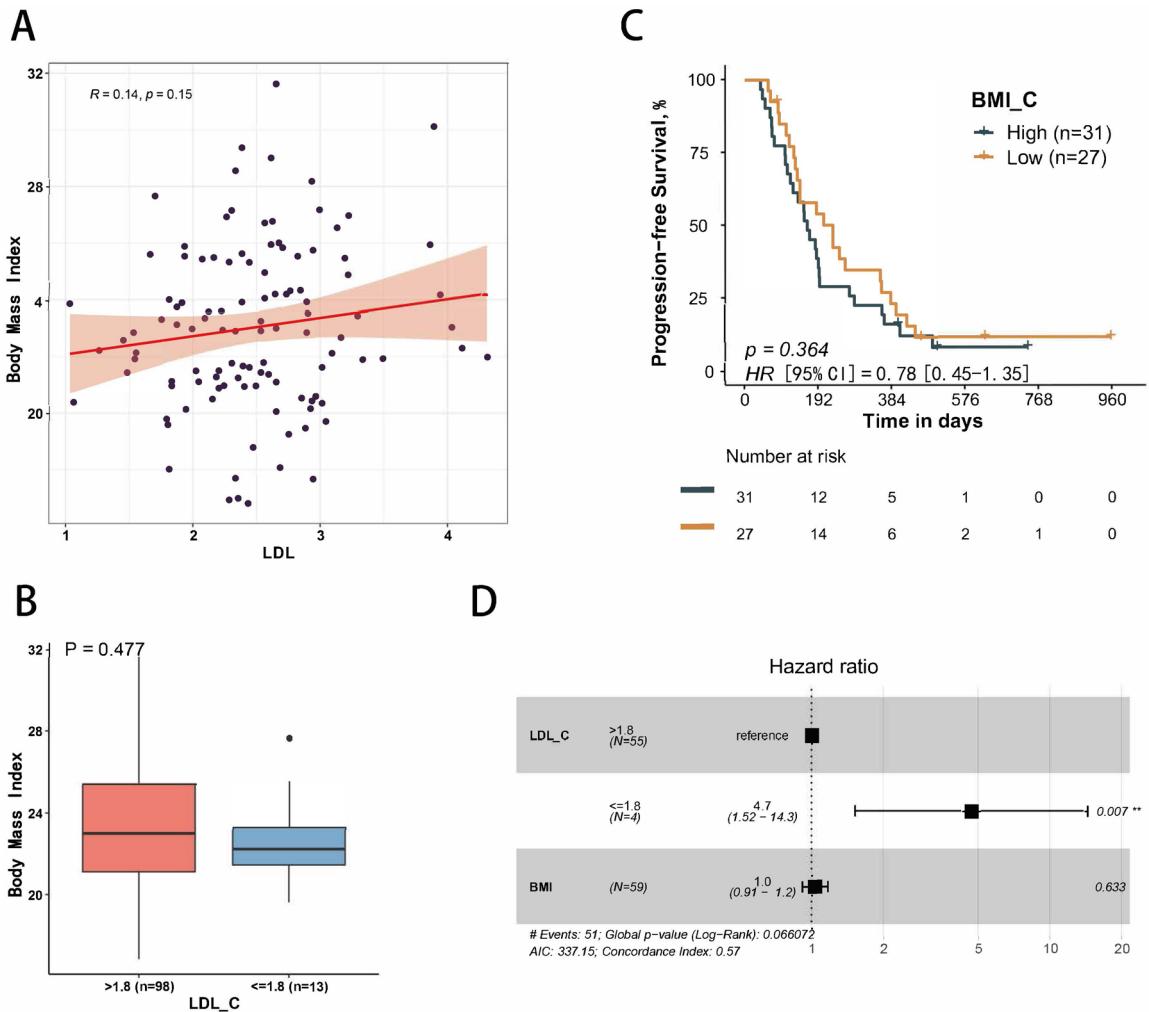


Figure S3 The correlation between BMI and LDL_C, as well as their influence on PFS in the first-line immunochemotherapy cohort. The study examined the relationship between BMI and LDL-C, as well as their impact on PFS in the cohort receiving ICI plus chemotherapy. Linear regression analysis indicated no significant correlation between BMI and LDL levels ($R=0.14$, $P=0.15$) (A). Similarly, no statistical difference in BMI was observed between the groups with LDL level of >1.8 mmol/L and those with level of ≤ 1.8 mmol/L (B). In the ICI plus chemotherapy cohort of this study, the median BMI was 22.63 kg/m^2 . Utilizing this cutoff, the cohort was stratified into two groups based on high and low BMI. No significant difference in PFS was detected between these two groups ($P=0.36$, $HR=0.78$, 95% CI: 0.45, 1.35) (C). To further clarify the impact of BMI and LDL on PFS in the ICI plus chemotherapy cohort, a multivariate Cox regression analysis was conducted. The results revealed that LDL-C levels independently and significantly differentiated the PFS of patients undergoing ICI plus chemotherapy, irrespective of their BMI (D). **, $P<0.05$. LDL, low-density lipoprotein; C, denotes the clinical features converted to categorical variables; BMI, body mass index; HR, hazard ratio; CI, confidence interval; AIC, Akaike information criterion; PFS, progression-free survival.

Table S2 A Cox regression model incorporating the interaction terms between the treatment modalities and potential biomarkers

Variables	Interaction_HR	Treatment_P value	Variables_P value	Interaction_P value	Interaction_Z value
LDL_C	5.567 (1.597–19.413)	0	0.697	0.007	2.694
Bone_M	0.391 (0.171–0.895)	0.567	0.864	0.026	-2.223
TC_C	2.173 (0.988–4.781)	0	0.013	0.054	1.93
NLR_C	0.519 (0.244–1.104)	0.114	0.734	0.089	-1.703
ApoA1	0.248 (0.049–1.265)	0.439	0.13	0.094	-1.677
CgA	0.532 (0.248–1.14)	0.061	0.966	0.105	-1.623
FIB_C	0.38 (0.112–1.285)	0.001	0.952	0.12	-1.556
Blood_sodium	1.093 (0.976–1.224)	0.099	0.46	0.123	1.543
LDH_C	0.532 (0.238–1.187)	0.059	0.491	0.123	-1.542
HDL	0.351 (0.084–1.468)	0.746	0.329	0.152	-1.434
NSE	1.005 (0.998–1.012)	0	0.748	0.161	1.401
Blood_sodium_C	2.617 (0.669–10.241)	0	0.629	0.167	1.382
KI_67	1.02 (0.991–1.049)	0.036	0.93	0.176	1.353
NSE_C	0.461 (0.146–1.456)	0.507	0.223	0.187	-1.32
PLT_C	1.689 (0.771–3.698)	0.001	0.996	0.19	1.311
TC	0.752 (0.487–1.16)	0.735	0.233	0.197	-1.289
CD56	2.326 (0.644–8.403)	0.01	0.041	0.198	1.288
TTF_1	1.922 (0.709–5.211)	0.002	0.054	0.199	1.284
NLR	1.176 (0.917–1.509)	0.003	0.449	0.201	1.28
sum_M	1.373 (0.839–2.248)	0	0.705	0.207	1.262
ApoB	0.287 (0.033–2.477)	0.848	0.373	0.256	-1.135
LDH	1.001 (0.999–1.002)	0	0.398	0.275	1.091
HDL_C	1.703 (0.641–4.524)	0	0.101	0.285	1.069
Neutrophil_C	0.671 (0.316–1.426)	0.03	0.14	0.3	-1.037
Cytokeratin_C	0.666 (0.307–1.444)	0.011	0.88	0.303	-1.03
Other_M	1.72 (0.566–5.229)	0.011	0.182	0.339	0.956
Lymphocyte	0.672 (0.293–1.544)	0.712	0.997	0.349	-0.936
Age	0.706 (0.334–1.492)	0.025	0.456	0.362	-0.911
Cytokeratin	1.05 (0.943–1.17)	0.001	0.671	0.374	0.889
PLT	0.998 (0.992–1.003)	0.666	0.679	0.377	-0.883
SYN	2.108 (0.396–11.225)	0.057	0.265	0.382	0.874
Monocyte_C	0.656 (0.225–1.912)	0.308	0.162	0.44	-0.772
Liver_M	0.734 (0.331–1.628)	0.061	0.873	0.447	-0.761
CEA	1.002 (0.996–1.008)	0	0.503	0.464	0.732
SEAA_C	1.568 (0.471–5.224)	0	0.408	0.464	0.732
Neutrophil	1.071 (0.886–1.294)	0.015	0.215	0.481	0.705
LDL	0.849 (0.476–1.515)	0.538	0.497	0.58	-0.553
Lymphocyte_C	1.205 (0.556–2.612)	0.004	0.305	0.636	0.473
ApoB_A_C	0.797 (0.268–2.373)	0.188	0.128	0.684	-0.407
TG	0.866 (0.424–1.769)	0.172	0.42	0.692	-0.395
CA19-9	1 (0.999–1.002)	0	0.771	0.722	0.355
FIB	1.034 (0.833–1.283)	0.066	0.49	0.764	0.301
Smoking	1.147 (0.442–2.974)	0.029	0.7	0.778	0.282
CA19-9_C	0.836 (0.236–2.962)	0	0.727	0.781	-0.278
Brain_M	0.851 (0.272–2.665)	0.186	0.972	0.782	-0.277
SEAA	0.952 (0.605–1.499)	0.02	0.66	0.832	-0.212
ApoB_A	1.157 (0.203–6.609)	0.159	0.458	0.869	0.164
Monocyte	1.057 (0.366–3.052)	0.022	0.666	0.919	0.102
KI_67_C	0.968 (0.353–2.649)	0	0.379	0.949	-0.064
ApoA1_C	0.973 (0.27–3.506)	0	0.061	0.967	-0.042
ApoB_C	1.012 (0.447–2.293)	0.006	0.164	0.978	0.028
TG_C	0.992 (0.463–2.124)	0.005	0.349	0.984	-0.02
CEA_C	1.003 (0.313–3.214)	0	0.96	0.996	0.005
Gender	0 (0–inf)	0.996	0.996	0.996	-0.005

HR, hazard ratio; LDL, low-density lipoprotein; C, denotes the clinical features converted to categorical variables; M, metastasis; TC, total cholesterol; NLR, neutrophil-to-lymphocyte ratio; ApoA1, apolipoprotein A1; CgA, chromogranin A; FIB, fibrinogen; LDH, lactate dehydrogenase; HDL, high-density lipoprotein; NSE, neuron-specific enolase; PLT, platelet; CD56, cluster of differentiation 56; TTF-1, thyroid transcription factor 1; sum_M, sum of tissues with metastatic lesions (e.g., brain, bone, liver, or other tissues); ApoB, apolipoprotein B; SYN, synuclein; CEA, carcinoembryonic antigen; SEAA, squamous epithelial associated antigen; TG, triglyceride; CA19-9, cancer antigen 19-9; inf, infinity.