



**Figure S1** Progression-free survival and overall survival of patients treated with ICI/chemotherapy or ICI/anti-angiogenic therapy. (A) Progression-free survival of patients treated with ICI/chemotherapy or ICI/anti-angiogenic therapy as the second-line or later treatment. (B) Overall survival of patients treated with ICI/chemotherapy or ICI/anti-angiogenic therapy as the second-line or later treatment. ICI, immune checkpoint inhibitor.

**Table S1** Univariate and multivariate Cox regression analyses of clinical parameters on PFS between ICI combination therapy and ICI monotherapy

Variable	Category	Univariate analysis		Multivariate analysis	
		HR (95% CI)	P	HR (95% CI)	P
Sex	Male vs. female	0.99 (0.64-1.53)	0.973	0.64 (0.25-1.68)	0.366
Age (years)	≥65 vs. <65	0.75 (0.50-1.10)	0.140	0.66 (0.44-0.99)	0.043
ECOG PS	2 vs. <2	1.47 (0.72-3.01)	0.295	1.49 (0.72-3.11)	0.285
Smoking histology	Smoker vs. never smoker	1.19 (0.79-1.79)	0.409	1.77 (0.70-4.45)	0.228
TNM stage	IV vs. III	1.49 (0.87-2.57)	0.146	1.65 (0.93-2.93)	0.089
Histology	Squamous vs. non-squamous	1.00 (0.70-1.43)	0.993	0.85 (0.58-1.24)	0.391
Treatment line	2 vs. ≥3	0.96 (0.63-1.48)	0.865	0.99 (0.62-1.59)	0.963
Therapeutic regimen	ICI combination therapy vs. ICI monotherapy	0.37 (0.26-0.53)	<0.001	0.35 (0.24-0.51)	<0.001

PFS, progression-free survival; ICI, immune checkpoint inhibitor; HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group performance status.

**Table S2** Univariate and multivariate Cox regression analyses of clinical parameters on OS between ICI combination therapy and ICI monotherapy

Variable	Category	Univariate analysis		Multivariate analysis	
		HR (95% CI)	P	HR (95% CI)	P
Sex	Male vs. female	1.18 (0.71-1.96)	0.519	1.33 (0.49-3.65)	0.578
Age (years)	≥65 vs. <65	0.88 (0.56-1.37)	0.562	0.86 (0.54-1.35)	0.503
ECOG PS	2 vs. <2	1.72 (0.80-3.73)	0.168	1.92 (0.86-4.28)	0.109
Smoking histology	Smoker vs. never smoker	1.18 (0.74-1.88)	0.491	1.06 (0.41-2.73)	0.899
TNM stage	IV vs. III	1.61 (0.85-3.02)	0.141	1.46 (0.76-2.81)	0.261
Histology	Squamous vs. non-squamous	0.94 (0.63-1.42)	0.777	0.79 (0.52-1.22)	0.289
Treatment line	2 vs. ≥3	0.70 (0.44-1.12)	0.136	0.71 (0.43-1.17)	0.179
Therapeutic regimen	ICI combination therapy vs. ICI monotherapy	0.41 (0.27-0.62)	<0.001	0.39 (0.26-0.60)	<0.001

OS, overall survival; ICI, immune checkpoint inhibitor; HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group performance status.

**Table S3** Univariate and multivariate Cox regression analyses of clinical parameters on PFS between ICI + C and ICI monotherapy

Variable	Category	Univariate analysis		Multivariate analysis	
		HR (95% CI)	P	HR (95% CI)	P
Sex	Male vs. female	1.07 (0.66-1.73)	0.781	0.71 (0.21-2.41)	0.586
Age (years)	≥65 vs. <65	0.77 (0.50-1.17)	0.217	0.65 (0.42-1.01)	0.054
ECOG PS	2 vs. <2	1.31 (0.61-2.83)	0.488	1.44 (0.66-3.16)	0.363
Smoking histology	Smoker vs. never smoker	1.19 (0.75-1.88)	0.453	1.71 (0.53-5.54)	0.369
TNM stage	IV vs. III	1.66 (0.91-3.03)	0.102	1.89 (0.98-3.65)	0.057
Histology	Squamous vs. non-squamous	0.87 (0.59-1.28)	0.481	0.81 (0.54-1.23)	0.329
Treatment line	2 vs. ≥3	1.05 (0.64-1.73)	0.854	1.12 (0.65-1.94)	0.681
Therapeutic regimen	ICI + C vs. ICI monotherapy	0.42 (0.29-0.63)	<0.001	0.38 (0.25-0.57)	<0.001

PFS, progression-free survival; ICI, immune checkpoint inhibitor; ICI + C, ICI plus chemotherapy; HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group performance status.

**Table S4** Univariate and multivariate Cox regression analyses of clinical parameters on OS between ICI + C and ICI monotherapy

Variable	Category	Univariate analysis		Multivariate analysis	
		HR (95% CI)	P	HR (95% CI)	P
Sex	Male vs. female	1.33 (0.75-2.37)	0.336	1.94 (0.54-7.01)	0.313
Age (years)	≥65 vs. <65	0.92 (0.57-1.48)	0.721	0.86 (0.52-1.41)	0.550
ECOG PS	2 vs. <2	1.61 (0.70-3.71)	0.264	1.95 (0.82-4.65)	0.131
Smoking histology	Smoker vs. never smoker	1.25 (0.73-2.14)	0.413	0.86 (0.26-2.86)	0.804
TNM stage	IV vs. III	1.87 (0.90-3.89)	0.094	1.80 (0.84-3.86)	0.133
Histology	Squamous vs. non-squamous	0.87 (0.56-1.36)	0.550	0.74 (0.46-1.19)	0.221
Treatment line	2 vs. ≥3	0.76 (0.44-1.30)	0.314	0.79 (0.44-1.41)	0.429
Therapeutic regimen	ICI + C vs. ICI monotherapy	0.40 (0.25-0.64)	<0.001	0.38 (0.24-0.62)	<0.001

OS, overall survival; ICI, immune checkpoint inhibitor; ICI + C, ICI plus chemotherapy; HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group performance status.

**Table S5** Univariate and multivariate Cox regression analyses of clinical parameters on PFS between ICI + A and ICI monotherapy

Variable	Category	Univariate analysis		Multivariate analysis	
		HR (95% CI)	P	HR (95% CI)	P
Sex	Male vs. female	0.97 (0.56-1.68)	0.904	0.51 (0.15-1.75)	0.283
Age (years)	≥65 vs. <65	0.69 (0.42-1.12)	0.132	0.59 (0.36-0.99)	0.047
ECOG PS	2 vs. <2	1.68 (0.67-4.21)	0.265	1.51 (0.60-3.84)	0.382
Smoking histology	Smoker vs. never smoker	1.32 (0.78-2.21)	0.302	2.24 (0.67-7.43)	0.189
TNM stage	IV vs. III	1.51 (0.77-2.94)	0.230	1.82 (0.88-3.79)	0.109
Histology	Squamous vs. non-squamous	1.02 (0.65-1.60)	0.936	0.79 (0.49-1.30)	0.359
Treatment line	2 vs. ≥3	1.08 (0.65-1.82)	0.759	0.97(0.53-1.80)	0.933
Therapeutic regimen	ICI + A vs. ICI monotherapy	0.30 (0.17-0.53)	<0.001	0.30 (0.17-0.53)	<0.001

PFS, progression-free survival; ICI, immune checkpoint inhibitor; ICI + A, ICI plus anti-angiogenic therapy; HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group performance status.

**Table S6** Univariate and multivariate Cox regression analyses of clinical parameters on OS between ICI + A and ICI monotherapy

Variable	Category	Univariate Analysis		Multivariate Analysis	
		HR (95% CI)	P	HR (95% CI)	P
Sex	Male vs. female	1.09 (0.61-1.98)	0.766	0.92 (0.26-3.29)	0.891
Age (years)	≥65 vs. <65	0.84 (0.50-1.44)	0.534	0.81 (0.47-1.4)	0.456
ECOG PS	2 vs. <2	2.03 (0.81-5.12)	0.133	2.10 (0.81-5.43)	0.125
Smoking histology	Smoker vs. never smoker	1.24 (0.71-2.15)	0.450	1.48 (0.44-5.00)	0.529
TNM stage	IV vs. III	1.86 (0.85-4.09)	0.122	1.75 (0.77-3.97)	0.180
Histology	Squamous vs. non-squamous	0.95 (0.59-1.54)	0.842	0.78 (0.47-1.30)	0.343
Treatment line	2 vs. ≥3	0.83 (0.48-1.43)	0.501	0.75 (0.41-1.36)	0.338
Therapeutic regimen	ICI + A vs. ICI monotherapy	0.44 (0.24-0.80)	0.007	0.43 (0.23-0.80)	0.008

OS, overall survival; ICI, immune checkpoint inhibitor; ICI + A, ICI plus anti-angiogenic therapy; HR, hazard ratio; ECOG, Eastern Cooperative Oncology Group performance status.