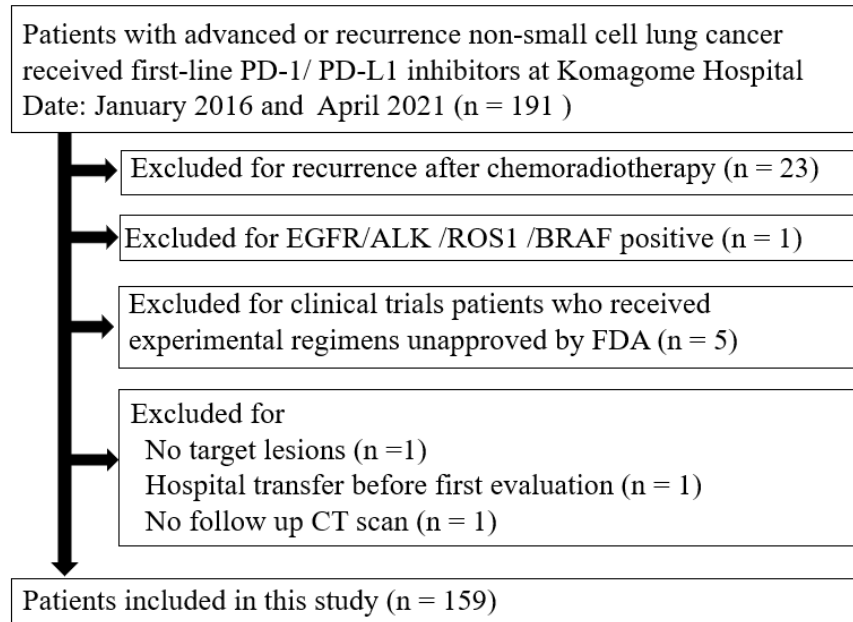


## Patient flow diagram

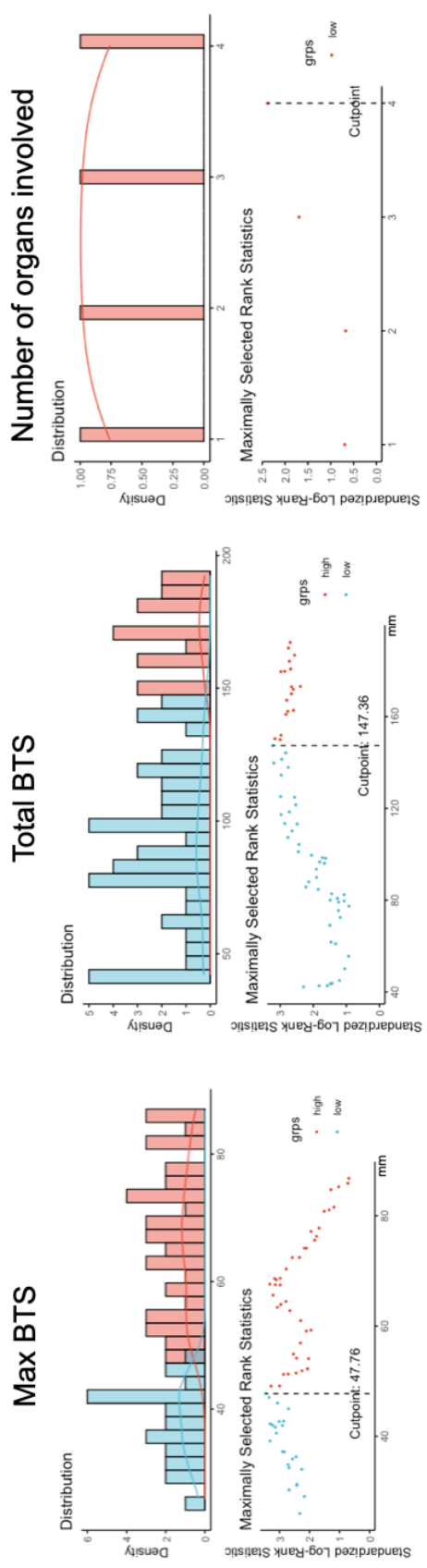


**Figure S1** Study flowchart. PD-1, programmed death-1; PD-L1, programmed death ligand-1.

**Table S1** Site of the largest target lesions

Site of the largest target lesions	ICI-mono (n=80), n (%)	ICI-chemo (n =79), n (%)	P
Primary lesion	57 (70.4)	55 (69.6)	0.135
Bone	4 (5.0)	7 (8.9)	–
Intrathoracic lymph node	3 (3.7)	5 (6.3)	–
Pleura	6 (7.4)	2 (2.5)	–
Brain	0 (0.0)	3 (3.8)	–
Adrenal gland	4 (5.0)	2 (2.5)	–
Lung (metastasis)	0 (0.0)	2 (2.5)	–
Others	4 (5.0)	2 (2.5)	–
Liver	0 (0.0)	1 (1.3)	–
Extrathoracic lymph node	3 (3.7)	0 (0.0)	–

ICI, immune checkpoint inhibitor; ICI-mono, ICI monotherapy; ICI-chemo, ICI in combination with chemotherapy.



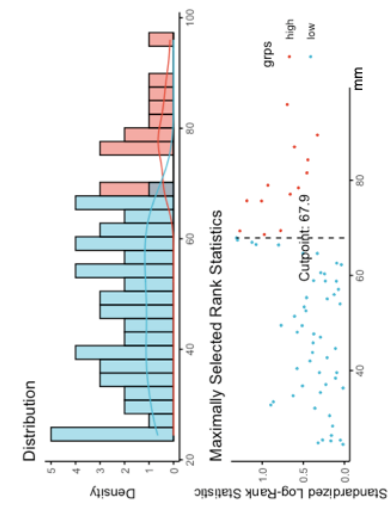
**Figure S2** Evaluating the cutoff points of patients who received ICI-mono using the minimum P value method (n=80). ICI, immune checkpoint inhibitor; ICI-mono, ICI monotherapy; BTS, baseline tumor size; max BTS, maximum BTS.

**Table S2** Characteristics of patients who received ICI-mono stratified by max BTS (n=80)

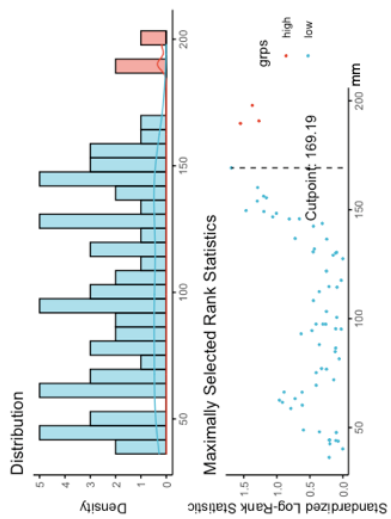
Characteristics	Small max BTS (n=30)	Large max BTS (n=50)	P
Median age [range], year	76.5 [46–87]	72 [46–87]	0.056
Sex, n (%)			0.489
Men	25 (75.0)	37 (74.0)	
Women	5 (25.0)	13 (26.0)	
Smoking status, n (%)			1.000
Brinkman index $\geq$ 400	23 (76.7)	37 (74.0)	
ECOG-PS, n (%)			0.254
0 or 1	22 (73.3)	29 (58.0)	
$\geq$ 2	8 (26.7)	21 (42.0)	
Histological subtypes, n (%)			0.427
Adenocarcinoma	21 (70.0)	28 (56.0)	
Squamous cell carcinoma	5 (16.7)	14 (28.0)	
NSCLC, NOS	4 (13.3)	8 (16.0)	
Staging, n (%)			0.452
Recurrence	12 (40.0)	12 (24.0)	
3	1 (3.3)	4 (8.0)	
4A	5 (16.7)	10 (20.0)	
4B	12 (40.0)	24 (48.0)	
Presence of brain metastasis, n (%)	6 (20.0)	10 (20.0)	1.000
Presence of bone metastasis, n (%)	10 (33.3)	20 (40.0)	0.721
Presence of liver metastasis, n (%)	3 (10.0)	10 (20.0)	0.389
PD-L1 expression, n (%)			0.518
<1%	0 (0.0)	0 (0.0)	
1–49%	6 (20.0)	6 (12.0)	
$\geq$ 50%	24 (80.0)	44 (88.0)	
Unknown	0 (0.0)	0 (0.0)	
Treatment regimen, n (%)			1.000
Atezolizumab (monotherapy)	0 (0.0)	0 (0.0)	
Pembrolizumab (monotherapy)	30 (100.0)	50 (100.0)	
LIPI score, n (%)			0.038
Good	14 (46.7)	13 (26.0)	
Intermediate	11 (36.7)	33 (66.0)	
Poor	5 (16.7)	4 (8.0)	

ICI, immune checkpoint inhibitor; ICI-mono, ICI monotherapy; BTS, baseline tumor size; max BTS, maximum BTS; ECOG-PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer; NOS, not otherwise specified; PD-L1, programmed death ligand-1; LIPI, lung immune prognostic index.

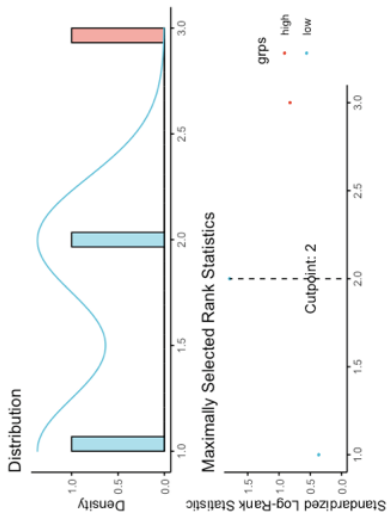
### Max BTS



### Total BTS



### Number of organs involved

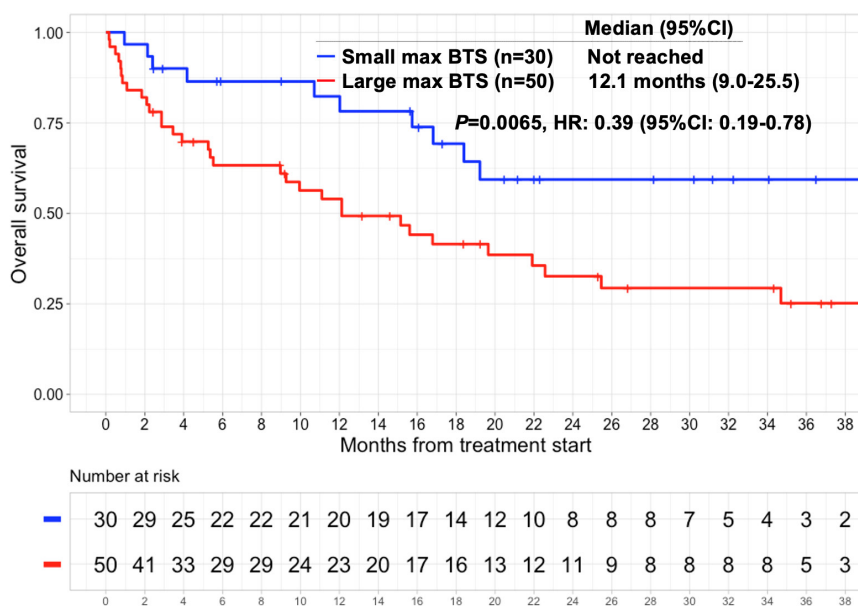


**Figure S3** Evaluating the cutoff point of patients who received ICI-chemo using the minimum P value method (n=79). ICI, immune checkpoint inhibitor; ICI-chemo, ICI in combination with chemotherapy; BTS, baseline tumor size; max BTS, maximum BTS.

**Table S3** Characteristics of patients who received ICI-chemo stratified by max BTS (n=79)

Characteristics	Small max BTS (n=58)	Large max BTS (n=21)	P
Median age [range], year	69 [36–81]	66 [31–75]	0.129
Sex, n (%)			0.042
Men	45 (77.6)	21 (100.0)	
Women	13 (22.4)	0 (0.0)	
Smoking status, n (%)			0.991
Brinkman index $\geq$ 400	45 (77.6)	17 (81.0)	
ECOG-PS, n (%)			1.000
0 or 1	57 (98.2)	20 (95.2)	
$\geq$ 2	1 (1.7)	1 (4.8)	
Histological subtypes, n (%)			0.346
Adenocarcinoma	43 (74.1)	12 (57.1)	
Squamous cell carcinoma	12 (20.7)	7 (33.3)	
NSCLC, NOS	3 (5.2)	2 (9.5)	
Staging, n (%)			0.130
Recurrence	8 (13.8)	0 (0.0)	
3	5 (8.6)	0 (0.0)	
4A	20 (34.5)	9 (42.9)	
4B	25 (43.1)	12 (57.1)	
Presence of brain metastasis, n (%)	9 (15.5)	4 (19.0)	0.978
Presence of bone metastasis, n (%)	22 (37.9)	8 (38.1)	1.000
Presence of liver metastasis, n (%)	7 (12.1)	1 (4.8)	0.600
PD-L1 expression, n (%)			0.991
<1%	18 (31.0)	6 (28.6)	
1–49%	15 (25.9)	6 (28.6)	
$\geq$ 50%	13 (22.4)	5 (23.8)	
Unknown	12 (20.7)	4 (19.0)	
Treatment regimen, n (%)			0.08
Pembrolizumab + platinum + pemetrexed	37 (63.8)	12 (57.1)	
Pembrolizumab + carboplatin + nab-paclitaxel	16 (27.6)	6 (28.6)	
Atezolizumab + carboplatin + paclitaxel + bevacizumab	3 (5.2)	2 (9.5)	
Atezolizumab + carboplatin + nab-paclitaxel	2 (3.4)	1 (4.8)	
LIPi score			0.036
Good	33 (56.9)	6 (28.6)	
Intermediate	22 (37.9)	11 (52.4)	
Poor	3 (5.2)	4 (19.0)	

ICI, immune checkpoint inhibitor; ICI-chemo, ICI in combination with chemotherapy; BTS, baseline tumor size; max BTS, maximum BTS; ECOG-PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer; NOS, not otherwise specified; PD-L1, programmed death ligand-1; LIPi, lung immune prognostic index; IQR, interquartile range.

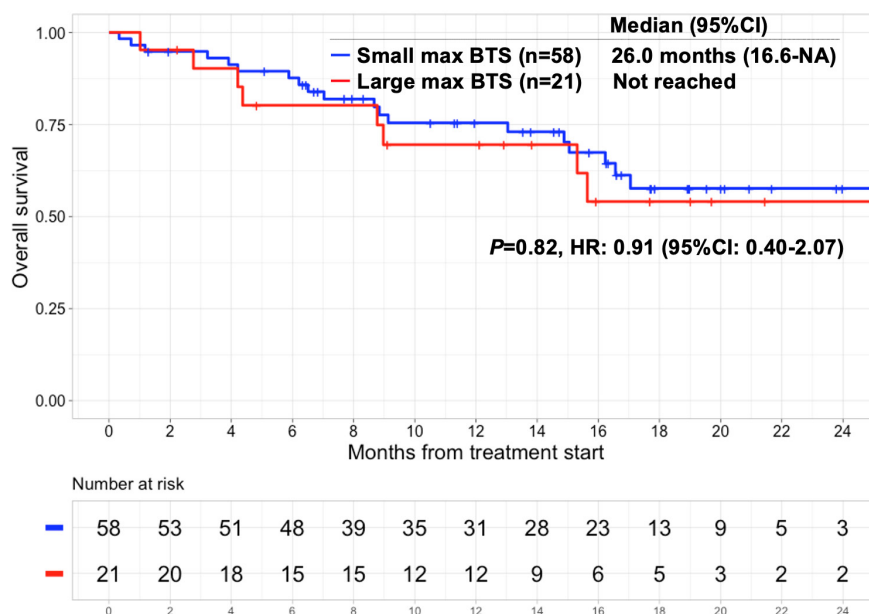


**Figure S4** Kaplan-Meier estimates of the OS of patients who received ICI-mono (n=80). Comparison between the small and large max BTS groups. OS, overall survival; ICI, immune checkpoint inhibitor; ICI-mono, ICI monotherapy; BTS, baseline tumor size; max BTS, maximum BTS; HR, hazard ratio; CI, confidence interval.

**Table S4** Best overall response to ICI-mono stratified by max BTS (n=80)

Response	Total (n=80)	Small max BTS (n=30)	Large-max BTS (n=50)	P
CR (%)	25	6.7	0.0	–
PR (%)	37.5	36.7	38.0	–
SD (%)	22.5	40.0	12.0	–
PD (%)	37.5	16.7	50.0	–
ORR (%)	40.0	43.4	38.0	0.284
DCR (%)	62.5	83.4	50.0	0.004

ICI, immune checkpoint inhibitor; ICI-mono, ICI monotherapy; BTS, baseline tumor size; max BTS, maximum BTS; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ORR, overall response rate; DCR, disease control rate.

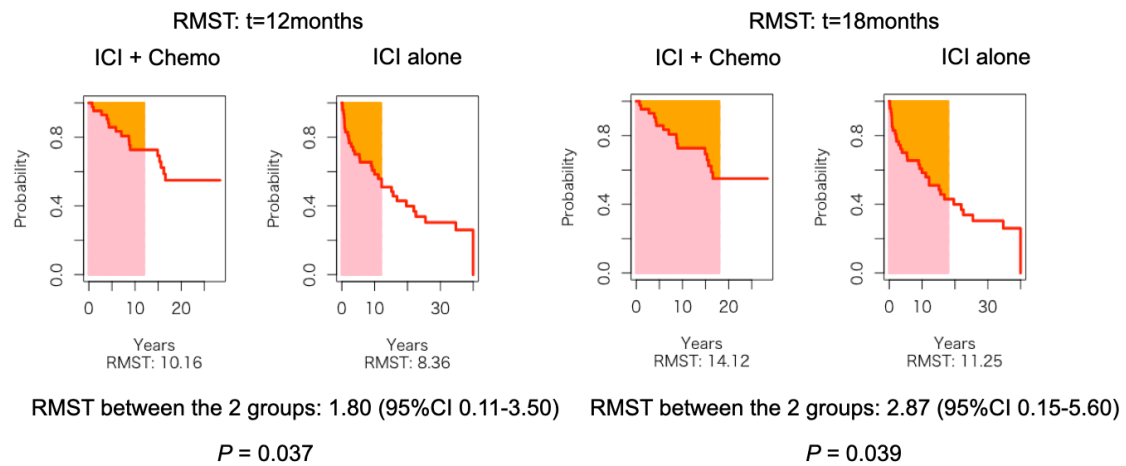


**Figure S5** Kaplan-Meier estimates of the OS of patients who received ICI-chemo (n=79). Comparison between the small and large max BTS groups. OS, overall survival; ICI, immune checkpoint inhibitor; ICI-chemo, ICI in combination with chemotherapy; BTS, baseline tumor size; max BTS, maximum BTS; HR, hazard ratio; CI, confidence interval.

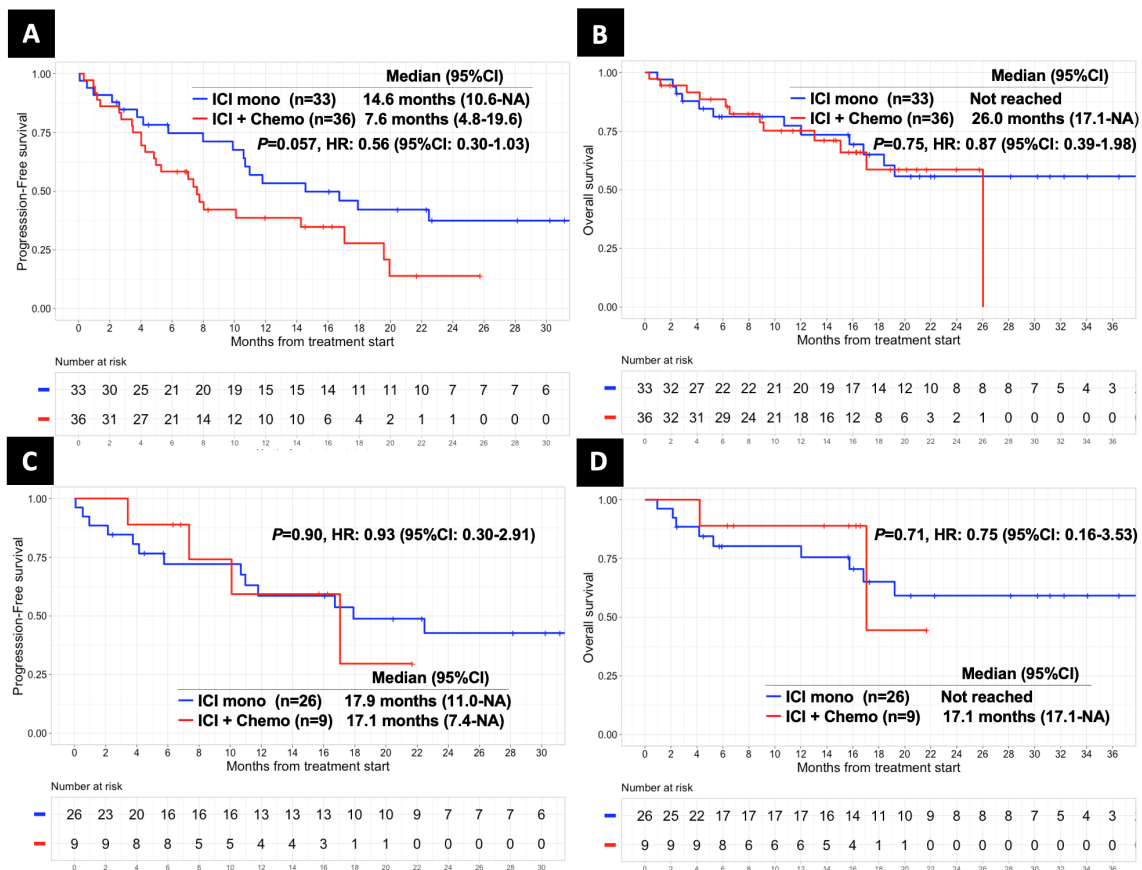
**Table S5** Best overall response to ICI-chemo stratified by max BTS (n=79)

Response	Total (n=79)	Small max BTS (n=58)	Large max BTS (n=21)	P
CR (%)	0.0	0.0	0.0	–
PR (%)	62.0	56.9	76.2	–
SD (%)	22.8	25.9	14.3	–
PD (%)	15.2	17.2	9.5	–
ORR (%)	62.0	56.9	76.2	0.189
DCR (%)	84.8	82.8	90.5	0.494

ICI, immune checkpoint inhibitor; ICI-chemo, ICI in combination with chemotherapy; BTS, baseline tumor size; max BTS, maximum BTS; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ORR, overall response rate; DCR, disease control rate.



**Figure S6** RMST estimates of the OS of patients with max BTS  $\geq 50$  mm (n=90). RMST, restricted mean survival time; ICI, immune checkpoint inhibitor; BTS, baseline tumor size; max BTS, maximum BTS; CI, confidence interval.



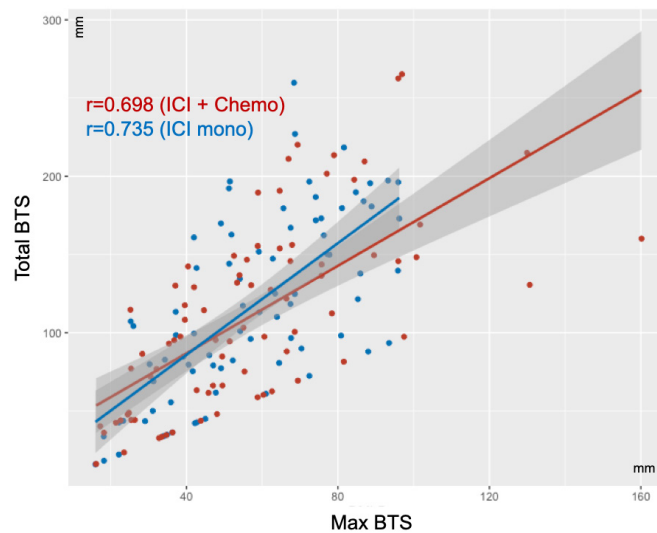
**Figure S7** Comparison of the Kaplan-Meier estimates of patients with max BTS  $< 50$  mm who received ICI-mono and ICI-chemo. (A) PFS (n=69). (B) OS (n=69). (C) PFS with PD-L1 score  $\geq 50\%$  group (n=35). (D) OS with PD-L1 score  $\geq 50\%$  group (n=35). BTS, baseline tumor size; max BTS, maximum BTS; ICI, immune checkpoint inhibitor; ICI-mono, ICI monotherapy; ICI-chemo, ICI in combination with chemotherapy; PD-L1, programmed death ligand-1; HR, hazard ratio; CI, confidence interval.



**Table S6** Univariate and multivariable analysis of the PFS of patients with max BTS <50 mm (n=69)

Variables	Univariate analysis			Multivariable analysis <sup>1</sup>		
	HR	95% CI	P	HR	95% CI	P
ICI-mono vs. ICI-chemo	0.55	0.30–1.02	0.057	0.56	0.28–1.13	0.107
Number of organs involved (<3 vs. ≥3)	0.98	0.53–1.80	0.949	0.52	0.26–1.04	0.065
PD-L1 TPS (≥50% vs. other)	0.42	0.23–0.79	0.007	0.48	0.22–1.01	0.053
Histological types (non-squamous vs. squamous)	0.26	0.13–0.54	<0.001	0.23	0.26–0.50	<0.001
LIPI score (good vs. other)	0.91	0.50–1.10	0.753	NA	NA	NA
ECOG-PS (<2 vs. ≥2)	1.08	0.45–2.56	0.864	NA	NA	NA
Sex (male vs. female)	0.89	0.41–1.94	0.780	NA	NA	NA
Age (<75 vs. ≥75)	0.69	0.38–1.27	0.236	NA	NA	NA
Smoking status (Brinkman index <400 vs. ≥400)	0.97	0.46–2.01	0.927	NA	NA	NA

<sup>1</sup>, type of ICI treatment, PD-L1 TPS, variables with P<0.20 in the univariate analysis were included. PFS, progression-free survival; BTS, baseline tumor size; max BTS, maximum BTS; ICI, immune checkpoint inhibitor; ICI-mono, ICI monotherapy; ICI-chemo, ICI in combination with chemotherapy; PD-L1, programmed death ligand-1; TPS, tumor proportion score; LIPI, lung immune prognostic index; ECOG-PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; CI, confidence interval; NA, not available.



**Figure S8** Correlative analysis of the max BTS and total BTS. The Spearman correlation coefficient (r) for the max BTS and total BTS in the ICI-mono group was 0.735 (P<0.0001). The Spearman correlation coefficient (r) for the max BTS and total BTS in the ICI-chemo group was 0.698 (P<0.0001). BTS, baseline tumor size; max BTS, maximum BTS; ICI, immune checkpoint inhibitor; ICI-mono, ICI monotherapy; ICI-chemo, ICI in combination with chemotherapy.