Table S1 Comparison of baseline characteristics among treatment groups

	Total	Cytotoxic chemotherapy	Targeted therapy	Immunotherapy	P value
Number of patients	1470 (100)	723 (49.2)	678 (46.1)	69 (4.7)	
Age	63.7±11.0	64.3±10.1	62.9±12.0	64.4±10.1	0.052
Male sex	869 (59.1)	558 (77.2)	261 (38.5)	50 (72.5)	<0.001
Pathology					<0.001
Adenocarcinoma	1219 (82.9)	517 (71.5)	657 (96.9)	45 (65.2)	
Squamous cell carcinoma	194 (13.2)	166 (23.0)	11 (1.6)	17 (24.6)	
NOS	26 (1.8)	14 (1.9)	8 (1.2)	4 (5.8)	
Others	31 (2.1)	26 (3.6)	2 (0.3)	3 (4.3)	
EGFR					<0.001
Wild Type	670 (45.6)	538 (74.4)	71 (10.5)	61 (88.4)	
Mutation	630 (42.9)	29 (4.0)	600 (88.5)	1 (1.4)	
Unknown	170 (11.6)	156 (21.6)	7 (1.0)	7 (10.1)	
ALK					<0.001
Wild Type	1141 (77.6)	521 (72.1)	558 (82.3)	62 (90.0)	
Mutation	94 (6.4)	27 (3.7)	67 (9.9)	0 (0.0)	
Unknown	235 (16.0)	175 (24.2)	53 (7.8)	7 (10.1)	
PD-L1					<0.001
Negative	210 (14.3)	99 (13.7)	98 (14.5)	13 (18.8)	
Positive	618 (42.0)	341 (47.2)	239 (35.3)	38 (55.1)	
Unknown	642 (43.7)	283 (39.1)	341 (50.3)	18 (26.1)	

NOS, not otherwise specified; EGFR, epidermal growth factor receptor; ALK, anaplastic lymphoma kinase; PD-L1, programmed death-ligand.

Table S2 PD-L1 status in the immunotherapy group

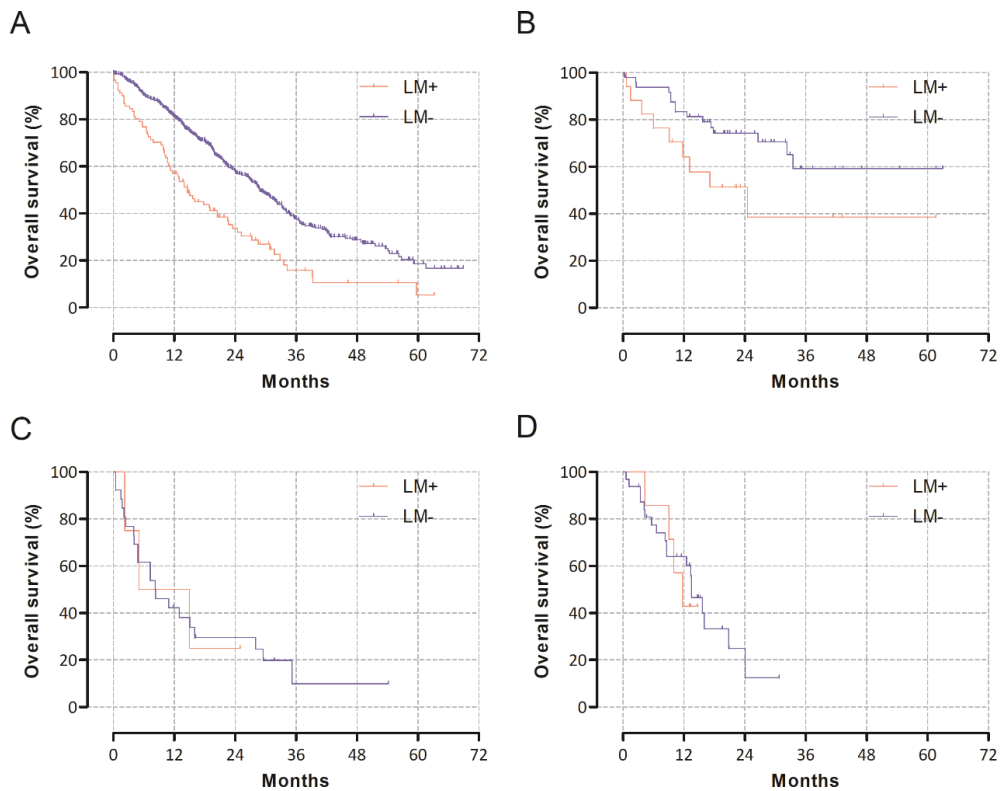|	Total (n=69)	Liver metastasis (n=11)	No liver metastasis (n=58)
≥50%	27 (39.1)	5 (45.5)	22 (37.9)
1–49%	11 (15.9)	2 (18.2)	9 (15.5)
<1%	13 (18.8)	2 (18.2)	11 (19.0)
Unknown	18 (26.1)	2 (18.2)	16 (27.6)

PD-L1, programmed death-ligand 1.

Figure S1 Subgroup analysis for overall survival with respect to liver metastasis. (A) EGFR-TKI subgroup in the targeted therapy group, P<0.001 [median OS: 14.6 (LM+) *vs*. 28.8 months (LM–)]. (B) ALK-TKI subgroup in the targeted therapy group, P=0.041 [median OS: 24.5 (LM+) *vs*. N/E months (LM–)]. (C) Immunotherapy alone subgroup in the immunotherapy group, P=0.944 [median OS: 10.1 (LM+) *vs*. 8.4 months (LM–)]. (D) Combination therapy subgroup in the immunotherapy group, P=0.772 [median OS: 11.7 (LM+) *vs*. 13.5 months (LM–)]. EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitors; OS, overall survival; LM, liver metastasis; ALK, anaplastic lymphoma kinase.
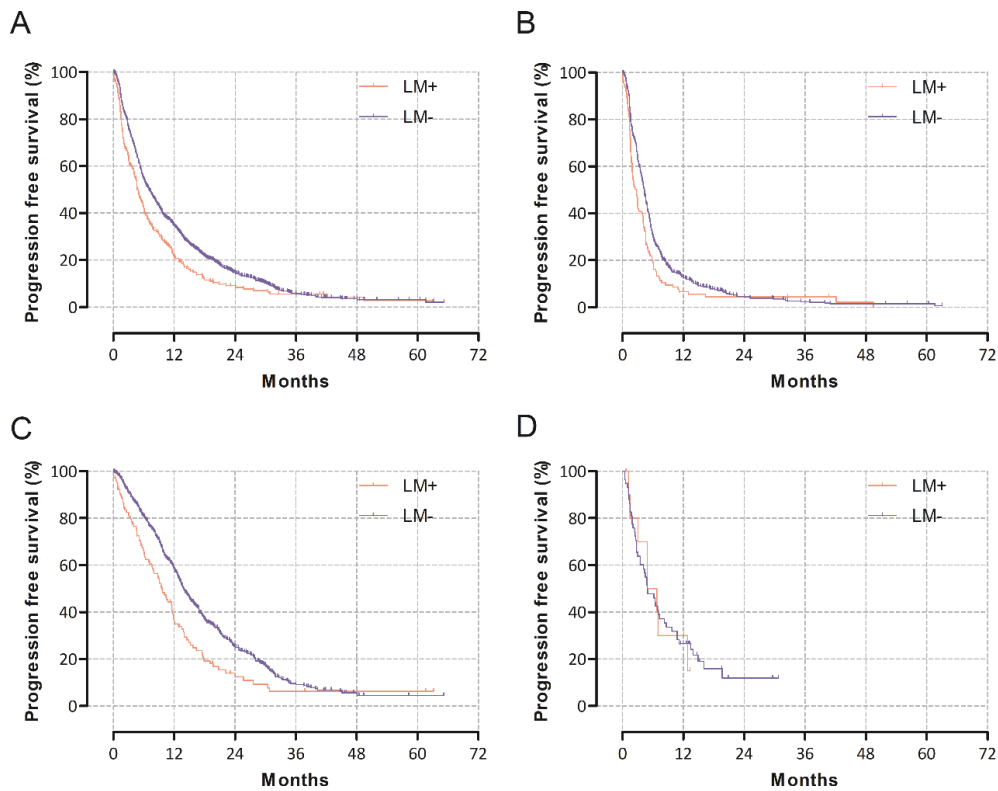
Figure S2 Progression-free survival according to liver metastasis. (A) Entire study population (P<0.001, median PFS: 4.7 (LM+) *vs*. 7.0 months (LM–)]. (B) Cytotoxic chemotherapy (P=0.002, median PFS: 2.8 (LM+) *vs*. 4.3 months (LM–)]. (C) Targeted therapy (P<0.001, median PFS: 9.6 (LM+) *vs*. 13.8 months (LM–)]. (D) Immunotherapy (P=0.955, median PFS: 4.9 (LM+) *vs*. 4.9 months (LM–)]. PFS, progression-free survival; LM, liver metastasis.
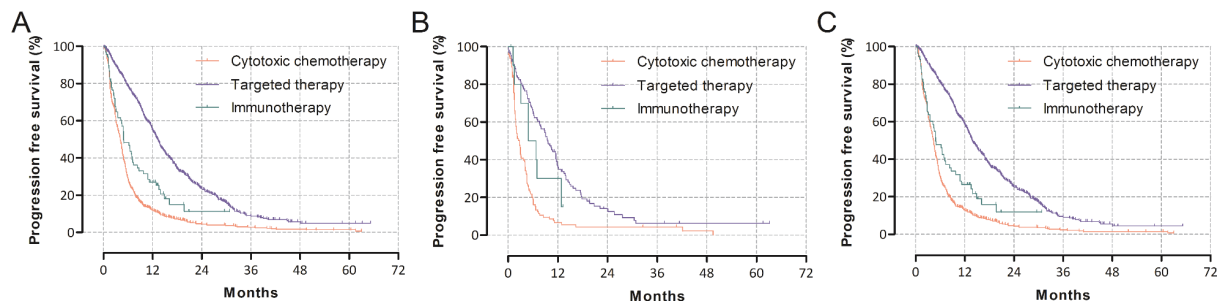
Figure S3 Progression-free survival according to treatment. (A) Entire population of metastatic NSCLC patients [P<0.001, median PFS: 4.1 (cytotoxic) *vs*. 13.3 (target) *vs*. 4.9 (IO) months]. (B) NSCLC with liver metastasis [P<0.001, median PFS: 2.8 (cytotoxic) *vs*. 9.6 (target) *vs*. 4.9 (IO) months]. (C) Metastatic NSCLC other than in the liver [P<0.001, median PFS: 4.3 (cytotoxic) *vs*. 13.8 (target) *vs*. 4.9 (IO) months]. NSCLC, non-small cell lung cancer; PFS, progression-free survival; IO, immunotherapy.
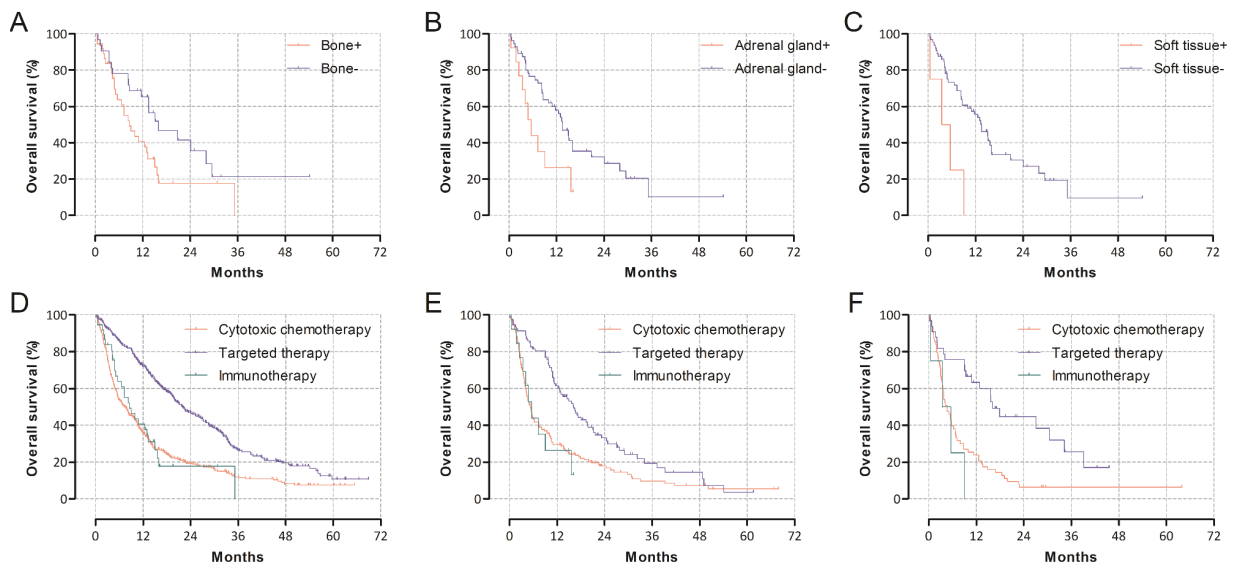

Figure S4 Overall survival with metastasis sites other than the liver. (A,B,C) Overall survival in patients who received immunotherapy with respect to the presence of metastasis (A. bone, P=0.033; B. adrenal gland, P=0.035; C. soft tissue, P=0.005). (D,E,F) Overall survival with respect to first-line chemotherapy (D. bone, P<0.001; E. adrenal gland, P<0.001; F. soft tissue metastasis, P<0.001).

Table S3 Cox regression analysis for progression-free survival

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	P value	HR	95% CI	P value
Age	1.008	1.003–1.013	0.003	1.006	1.000–0.011	0.049
Male sex	1.531	1.363–1.719	<0.001	1.155	1.018–1.311	0.026
Pathology						
Adenocarcinoma	1.000			1.000		
Squamous cell carcinoma	2.270	1.931–2.669	<0.001	1.619	1.261–2.078	<0.001
EGFR mutation	0.474	0.419–0.536	<0.001	0.420	0.366–0.482	<0.001
ALK mutation	0.733	0.572–0.939	0.014	0.424	0.323–0.557	<0.001
PD-L1 positive	1.147	0.966–1.361	0.119		Not retained	
Metastasis site						
Liver	1.356	1.165–1.579	<0.001	1.187	1.009–1.395	0.039
Contralateral lung	0.985	0.873–1.111	0.804		Not retained	
Extrathoracic lymph node	1.325	1.180–1.488	<0.001	1.086	0.945–1.248	0.245
Pleura	0.962	0.859–1.078	0.507		Not retained	
Bone	1.177	1.051–1.319	0.005	1.198	1.049–1.368	0.008
Brain	0.850	0.752–0.960	0.009	0.966	0.837–1.115	0.637
Adrenal gland	1.707	1.475–1.976	<0.001	1.462	1.250–1.710	<0.001
Soft tissue	1.542	1.241–1.916	<0.001	1.172	0.932–1.473	0.174
Number of metastatic sites						
One	1.000			1.000		
Two	1.156	0.994–1.343	0.060	1.034	0.884–1.210	0.676
More than three	1.397	1.220–1.599	<0.001	1.301	1.101–1.539	0.002

EGFR, epidermal growth factor receptor; ALK, anaplastic lymphoma kinase; PD-L1, programmed death-ligand 1; CI, confidence interval; HR, hazard ratio.