

Figure S1 Flow chart of patients' selection.

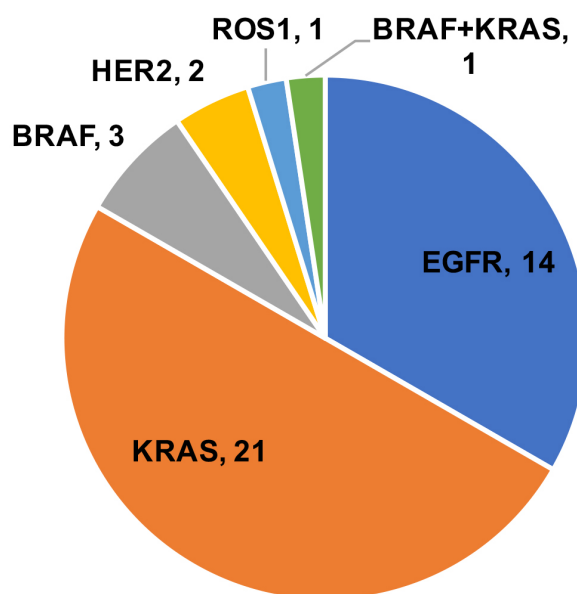


Figure S2 Mutations-testing results of 42 patients with genetic aberrations.

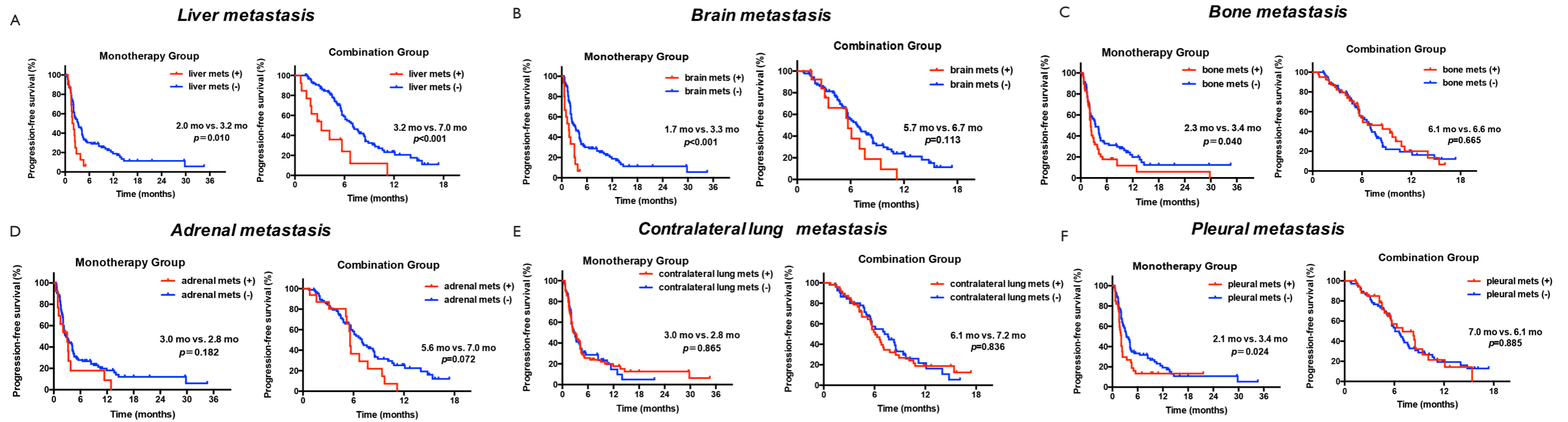


Figure S3 PFS in patients treated with ICI stratified by metastatic pattern. (A) Liver metastasis; (B) brain metastasis; (C) bone metastasis; (D) adrenal metastasis; (E) contralateral lung metastasis; (F) pleural metastasis. ICI, immune checkpoint inhibitor.

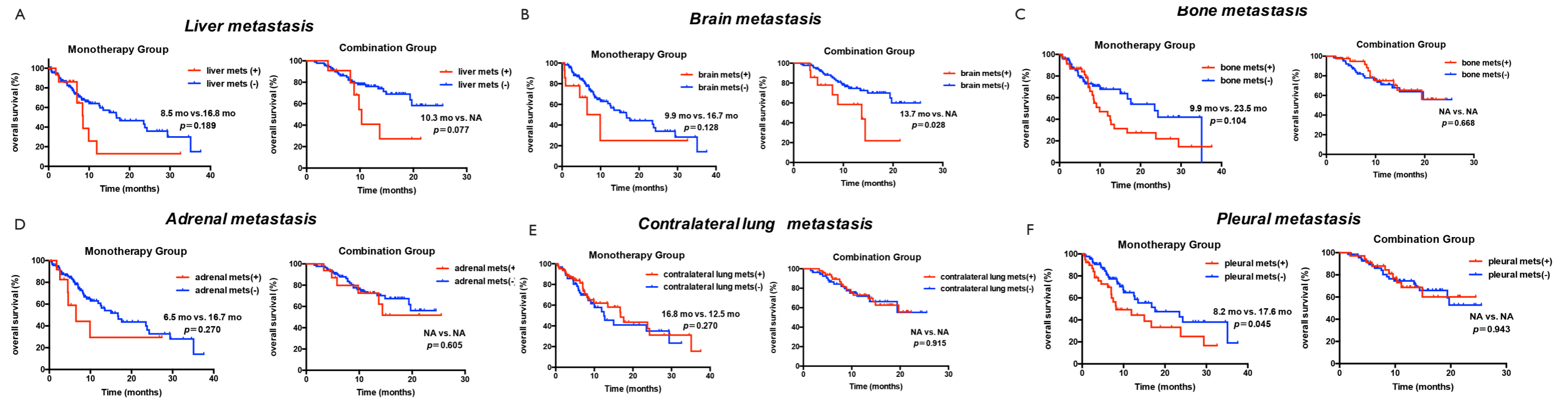
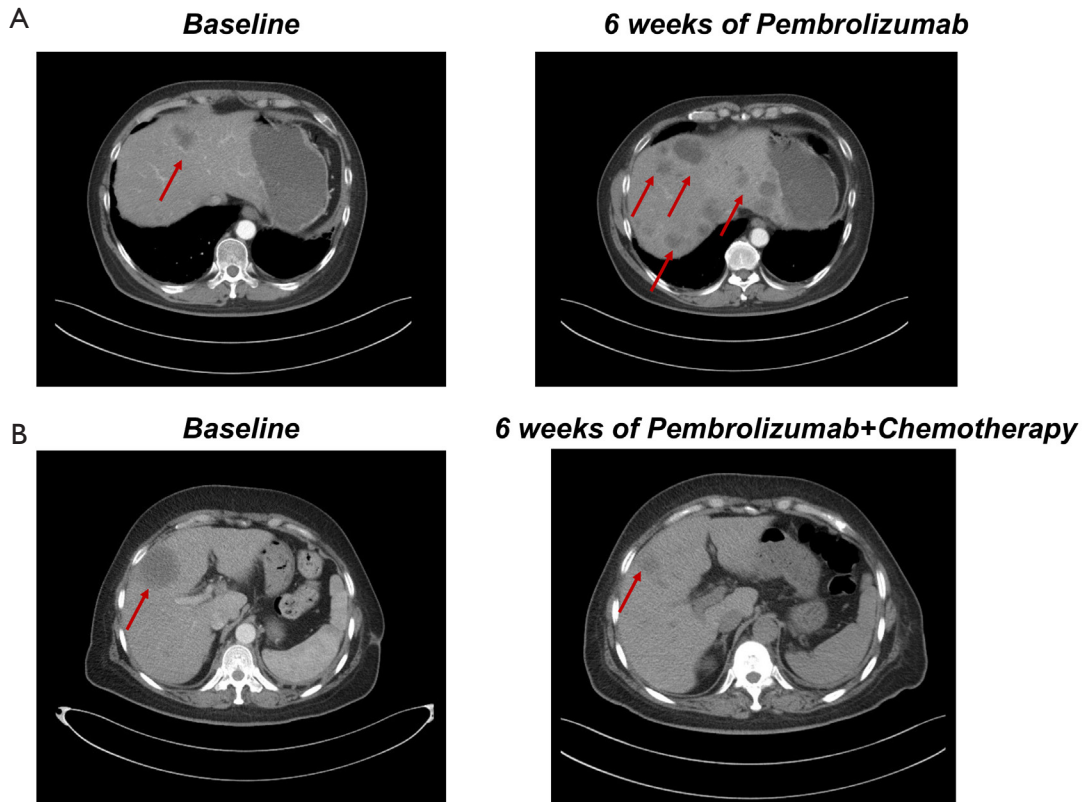
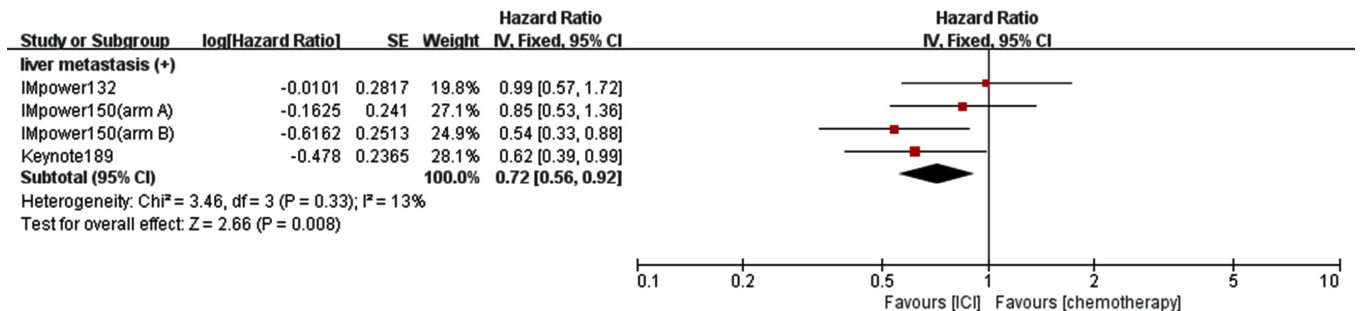


Figure S4 OS in patients treated with ICI stratified by metastatic pattern. (A) Liver metastasis; (B) brain metastasis; (C) bone metastasis; (D) adrenal metastasis; (E) contralateral lung metastasis; (F) pleural metastasis. ICI, immune checkpoint inhibitor.



**Figure S5** Representative intrahepatic response in patients with liver metastasis treated with ICI monotherapy or ICI combination therapy. (A) This male patient was diagnosed as stage IV lung squamous in March, 2017. After 4 cycles of chemotherapy, pulmonary lesion progressed. Therefore, the patient received pembrolizumab monotherapy as second-line treatment strategy. However, after two cycles of pembrolizumab, LM progressed but SD in pulmonary lesion was maintained; PFS was only 2.1 months. (B) This female patient was diagnosed as stage IV lung adenocarcinoma in January, Year 2019. This patient received combination therapy (pembrolizumab + pemetrexed + carboplatin) as first-line therapy. After two cycles of combination treatment, the patient exhibited partial response, with obviously shrunken hepatic lesions. At data cut-off, she was continuing to receive combination therapy with ongoing response. ICI, immune checkpoint inhibitor.



**Figure S6** Meta-analysis of trials with available subgroup data on LM. LM, liver metastasis.

**Table S1** Lists of treatment ICI treatment strategies

ICI	Combining strategy	No. of patients
ICI monotherapy		
Nivolumab	–	33
Pembrolizumab	–	71
Atezolizumab	–	1
SHR-1210	–	21
IBI308	–	2
ICI + chemotherapy		
Pembrolizumab	Pemetrexed	1
	Pemetrexed + carboplatin	9
	Pemetrexed + carboplatin + bevacizumab	1
	Gemcitabine + carboplatin	3
	Abraxane	7
	Abraxane + carboplatin	3
	Paclitaxel + carboplatin	1
Nivolumab	Pemetrexed + carboplatin	1
	Gemcitabine	1
	Abraxane	2
SHR-1210	Pemetrexed + carboplatin	30
JS001	Pemetrexed + carboplatin	5
ICI + anti-angiogenesis		
Pembrolizumab	Apatinib	2
	Bevacizumab	1
Nivolumab	Bevacizumab	1
SHR-1210	Apatinib	36

ICI, immune checkpoint inhibitor.

**Table S2** Patient characteristics according to LM status

Characteristic	Liver metastasis (+) (n=7)	Liver metastasis (-) (n=39)	P value
Median age, years (range)	62.5 (58 to 76)	61.5 (40 to 78)	0.717
Sex, n (%)			
Male	7 (100.0)	35 (89.7)	1.000
Female	0 (0.0)	4 (10.3)	
Smoking history, n (%)			0.313
Current/former	6 (85.7)	26 (66.7)	
Never	1 (14.3)	13 (33.3)	
Pathology, n (%)			0.626
Adenocarcinoma	4 (57.1)	26 (66.7)	
Others	3 (42.9)	13 (33.3)	
Staging, n (%)			0.496
IIIB-IV	6 (85.7)	36 (92.3)	
Post-operative recurrence	1 (14.3)	3 (7.7)	
Gene aberrations, n (%)			0.941
Wild-type	6 (85.7)	33 (84.6)	
Mutated	1 (14.3)	6 (15.4)	
Treatment strategy, n (%)			0.698
ICI alone	3 (42.9)	20 (51.3)	
ICI + chemotherapy	2 (28.6)	13 (33.3)	
ICI + anti-angiogenesis	2 (28.6)	6 (15.4)	
PD-L1 expression (IHC), n (%)			0.216
PD-L1 positive	1 (14.3)	15 (38.5)	
PD-L1 negative	6 (85.7)	24 (61.5)	
CD8 expression (IHC), n (%)			0.634
CD8 <sup>+</sup> TILs	5 (71.4)	31 (79.5)	
CD8 <sup>-</sup> TILs	2 (28.6)	8 (20.5)	

IHC, immunohistochemistry.