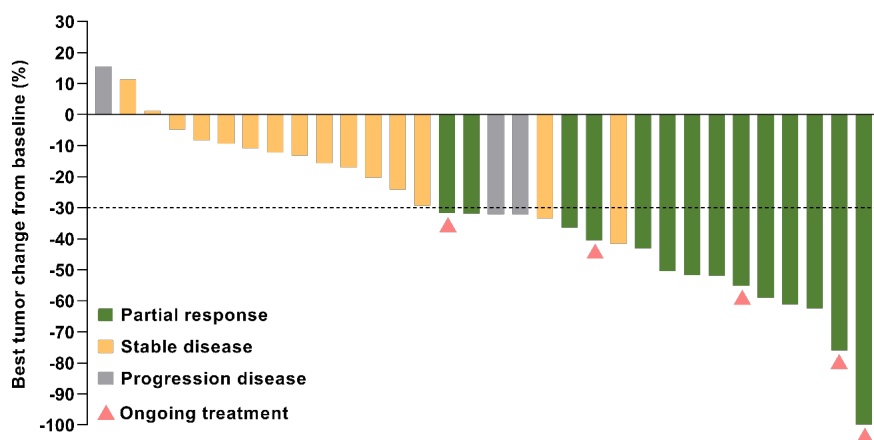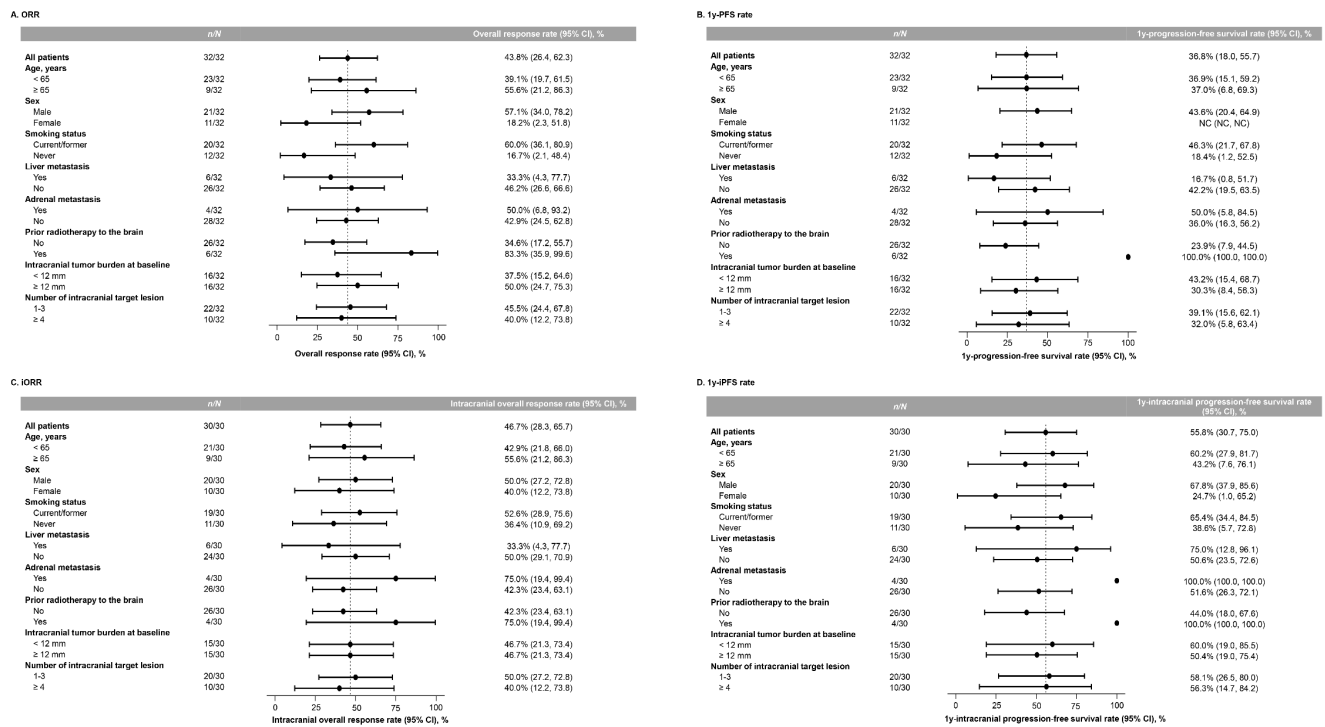**Figure S1** Flow diagram.

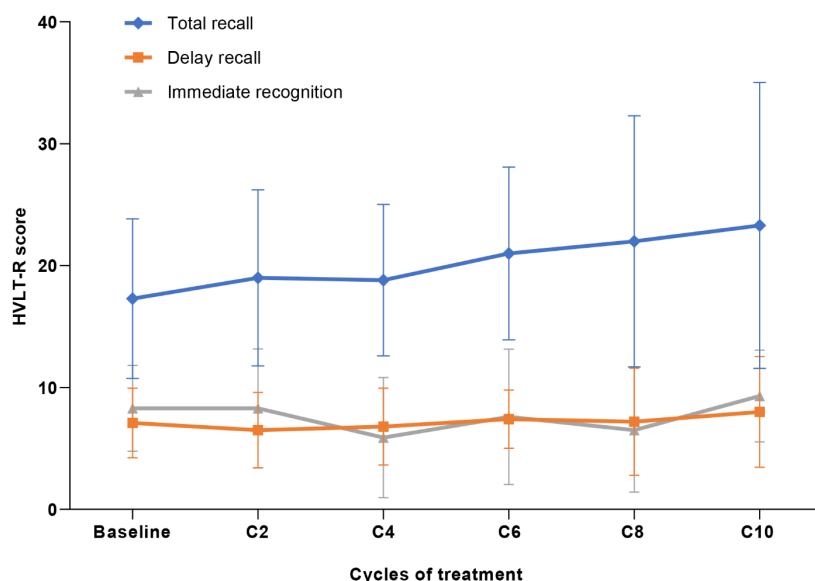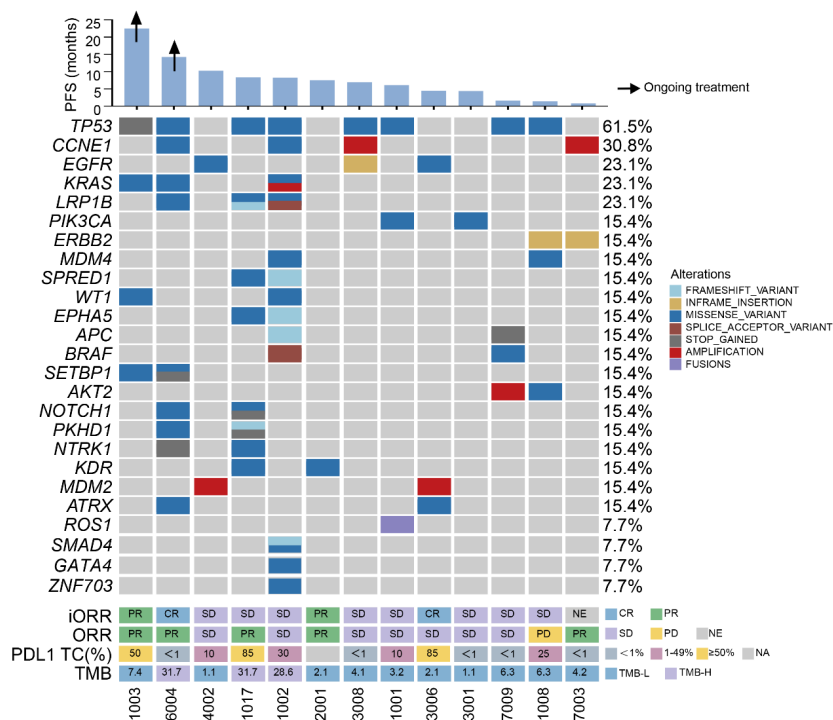**Figure S2** Waterfall plot for best percentage change in sums of diameters of target lesions from baseline in Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 efficacy analysis set (n=32). Best responses were assessed by RECIST v1.1. Each bar represents an individual patient. Two patients had progressive diseases (PD) despite >30% shrinkage of target lesions due to the development of new lesions in brain or liver.

A. ORR

	n/N	Overall response rate (95% CI), %
All patients	32/32	43.8% (26.4, 62.3)
Age, years		
<65	23/32	39.1% (19.7, 61.5)
≥65	9/32	55.6% (21.2, 86.3)
Sex		
Male	21/32	57.1% (34.0, 78.2)
Female	11/32	18.2% (2.3, 51.8)
Smoking status		
Current/former	20/32	60.0% (36.1, 80.9)
Never	12/32	16.7% (2.1, 48.4)
Liver metastasis		
Yes	6/32	33.3% (4.3, 77.7)
No	26/32	46.2% (26.6, 66.6)
Adrenal metastasis		
Yes	4/32	50.0% (6.8, 93.2)
No	28/32	42.9% (24.5, 62.8)
Prior radiotherapy to the brain		
No	26/32	34.6% (17.2, 55.7)
Yes	6/32	83.3% (35.9, 99.6)
Intracranial tumor burden at baseline		
<12 mm	16/32	37.5% (15.2, 64.6)
≥12 mm	16/32	50.0% (24.7, 75.3)
Number of intracranial target lesion		
1–3	22/32	45.5% (24.4, 67.8)
≥4	10/32	40.0% (12.2, 73.8)

Overall response rate (95% CI), %

B. 1y-PFS rate

	n/N	1y-progression-free survival rate (95% CI), %
All patients	32/32	36.8% (18.0, 55.7)
Age, years		
<65	23/32	36.9% (15.1, 59.2)
≥65	9/32	37.0% (6.8, 69.3)
Sex		
Male	21/32	43.6% (20.4, 64.9)
Female	11/32	NC (NC, NC)
Smoking status		
Current/former	20/32	46.3% (21.7, 67.8)
Never	12/32	18.4% (1.2, 52.5)
Liver metastasis		
Yes	6/32	16.7% (0.8, 51.7)
No	26/32	42.2% (19.5, 63.5)
Adrenal metastasis		
Yes	4/32	50.0% (5.8, 84.5)
No	28/32	36.0% (16.3, 56.2)
Prior radiotherapy to the brain		
No	26/32	23.9% (7.9, 44.5)
Yes	6/32	100.0% (100.0, 100.0)
Intracranial tumor burden at baseline		
<12 mm	16/32	43.2% (15.4, 68.7)
≥12 mm	16/32	30.3% (8.4, 58.3)
Number of intracranial target lesion		
1–3	22/32	39.1% (15.6, 62.1)
≥4	10/32	32.0% (5.8, 63.4)

1y-progression-free survival rate (95% CI), %

C. iORR

	n/N	Intracranial overall response rate (95% CI), %
All patients	30/30	46.7% (28.3, 65.7)
Age, years		
<65	21/30	42.9% (21.8, 66.0)
≥65	9/30	55.6% (21.2, 86.3)
Sex		
Male	20/30	50.0% (27.2, 72.8)
Female	10/30	40.0% (12.2, 73.8)
Smoking status		
Current/former	19/30	52.6% (28.9, 75.6)
Never	11/30	36.4% (10.9, 69.2)
Liver metastasis		
Yes	6/30	33.3% (4.3, 77.7)
No	24/30	50.0% (29.1, 70.9)
Adrenal metastasis		
Yes	4/30	75.0% (19.4, 99.4)
No	26/30	42.3% (23.4, 63.1)
Prior radiotherapy to the brain		
No	26/30	42.3% (23.4, 63.1)
Yes	4/30	75.0% (19.4, 99.4)
Intracranial tumor burden at baseline		
<12 mm	15/30	46.7% (21.3, 73.4)
≥12 mm	15/30	46.7% (21.3, 73.4)
Number of intracranial target lesion		
1–3	20/30	50.0% (27.2, 72.8)
≥4	10/30	40.0% (12.2, 73.8)

Intracranial overall response rate (95% CI), %

D. 1y-iPFS rate

	n/N	1y-intracranial progression-free survival rate (95% CI), %
All patients	30/30	55.8% (30.7, 75.0)
Age, years		
<65	21/30	60.2% (27.9, 81.7)
≥65	9/30	43.2% (7.6, 76.1)
Sex		
Male	20/30	67.8% (37.9, 85.6)
Female	10/30	24.7% (1.0, 65.2)
Smoking status		
Current/former	19/30	65.4% (34.4, 84.5)
Never	11/30	38.6% (5.7, 72.8)
Liver metastasis		
Yes	6/30	75.0% (12.8, 96.1)
No	24/30	50.6% (23.5, 72.6)
Adrenal metastasis		
Yes	4/30	100.0% (100.0, 100.0)
No	26/30	51.6% (26.3, 72.1)
Prior radiotherapy to the brain		
No	26/30	44.0% (18.0, 67.6)
Yes	4/30	100.0% (100.0, 100.0)
Intracranial tumor burden at baseline		
<12 mm	15/30	60.0% (19.0, 85.5)
≥12 mm	15/30	50.4% (19.0, 75.4)
Number of intracranial target lesion		
1–3	20/30	58.1% (26.5, 80.0)
≥4	10/30	56.3% (14.7, 84.2)

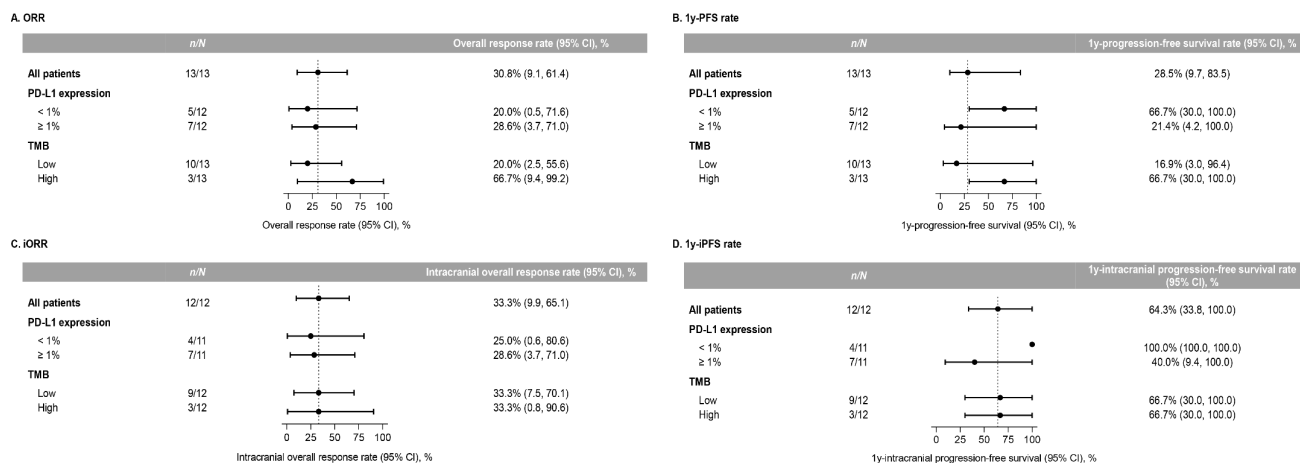1y-intracranial progression-free survival rate (95% CI), %

Figure S3 Subgroup analysis for systemic and intracranial efficacy by clinicopathological features. Forest plots show systemic objective response rate (A), 1-year progression-free survival rate (B), intracranial objective response rate (C) and 1-year intracranial PFS rate (D) by clinicopathological features. CI, confidence interval; ORR, objective response rate; PFS, progression-free survival; iORR, intracranial objective response rate; iPFS, intracranial progression-free survival.

Figure S4 Hopkins Verbal Learning Test-Revised (HVLT-R) Scores. Raw scores were derived from the cognitive assessments. Data were plotted as means plus or minus standard deviations.

Figure S5 Baseline mutation profiles, PD-L1 and TMB of patients. The heatmap depicts Top 25 mutated genes in this study. Reported frequencies include a composite of missense, nonsense, indel, splice mutations, copy-number variants and fusions for each gene. The top bar chart shows progression-free survival of each patient, and arrow indicates patients are still ongoing treatment. The clinical benefits (intracranial overall response rate, overall response rate), PD-L1 expression and TMB values are annotated in the bottom panel. PD-L1, programmed cell death protein-ligand 1; TMB, tumor mutational burden.

Figure S6 Subgroup analysis for systemic and intracranial efficacy by PD-L1 expression and TMB. Forest plots show systemic objective response rate (A), 1-year PFS rate (B), intracranial objective response rate (C) and 1-year iPFS rate (D) in PD-L1 or TMB subgroups. PD-L1, programmed cell death protein-ligand 1; TMB, tumor mutational burden; CI, confidence interval; ORR, objective response rate; PFS, progression-free survival; iORR, intracranial objective response rate; iPFS, intracranial progression-free survival.