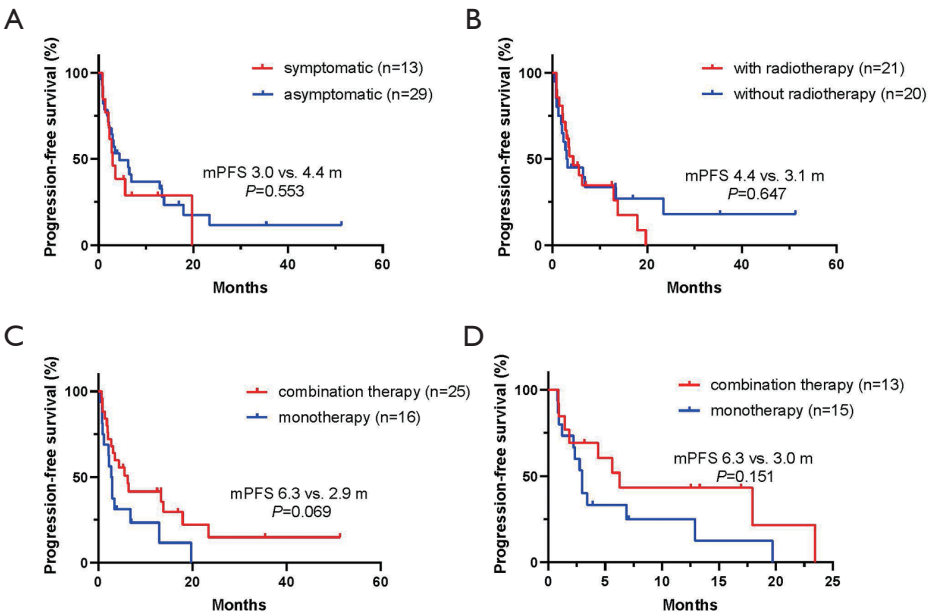


**Figure S1** PFS comparison in different subgroups of patients with BMs: patients who presented with or without neurological symptoms (A), patients who had received radiotherapy for intracranial lesion or not (B), patients who were treated with ICI monotherapy or combination therapy (C), patients who were treated with ICI monotherapy or combination therapy at posterior-line (D). PFS, progression-free survival; BMs, brain metastases; ICI, immune checkpoint inhibitor.

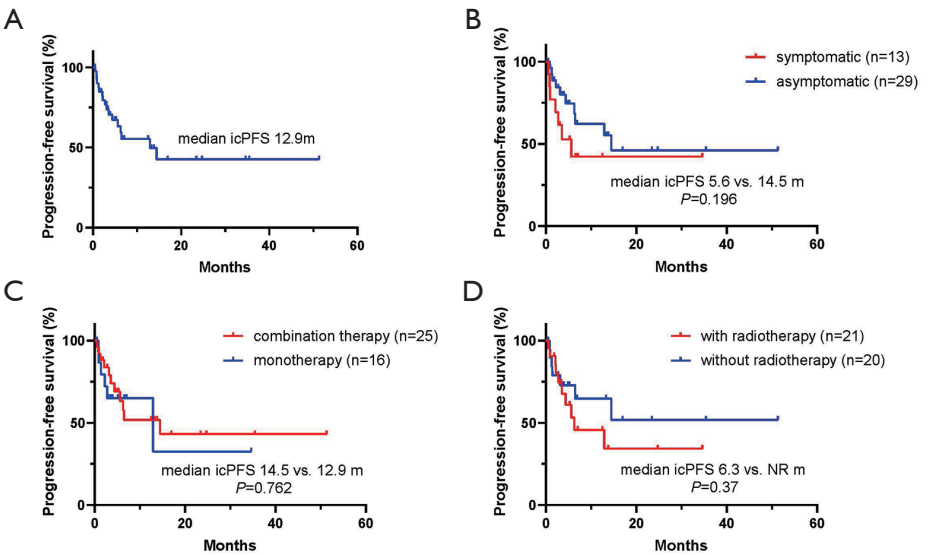


**Figure S2** icPFS of all patients with BMs (A). icPFS comparison in different subgroups of patients with BMs: patients who presented with or without neurological symptoms (B), patients who were treated with ICI monotherapy or combination therapy (C), patients who had received radiotherapy for intracranial lesion or not (D). icPFS intracranial progression-free survival; BMs, brain metastases; ICI, immune checkpoint inhibitor.

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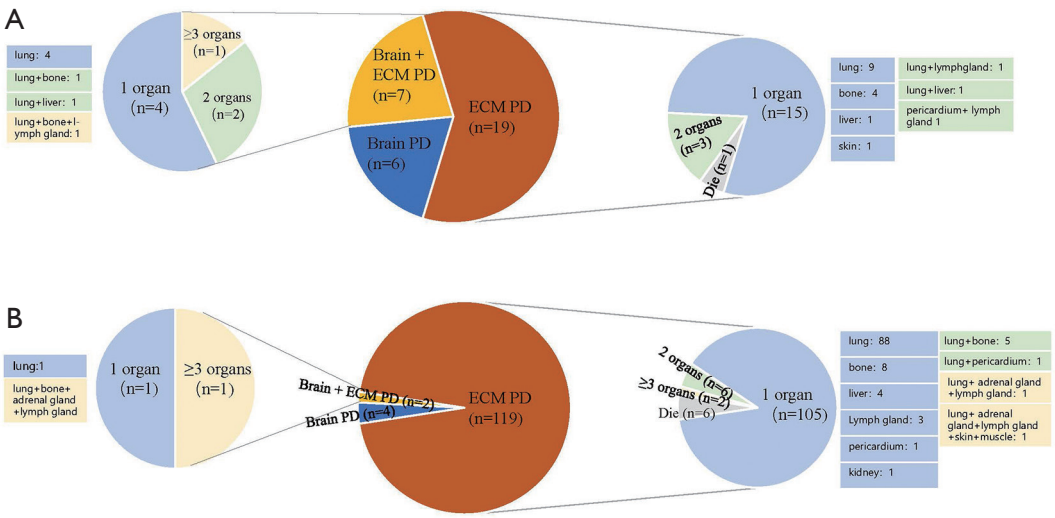


**Figure S3** Progression patterns of patients with (A) or without (B) BMs after ICI-based treatment. For patients presented as "ECM PD", the distribution of patients with different number of involved organs was showed in the right pie, and the table aside the pie listed the specific organs involved for each patient. For patients presented as "Brain + ECM PD", the distribution of patients with different number of organs involved in ECM PD was showed in the left pie, and the table aside the pie listed the specific organs for each patient. BMs, brain metastases; ICI, immune checkpoint inhibitor; ECM, extracranial metastases; PD, progression disease.

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**Table S1** Univariate and multivariate analysis of PFS in patients with BMs

| Factor | No. (%) | Univariate analysis | | | Multivariate analysis | |
|---|---|---|---|---|---|---|
| | | PFS | HR (95% CI) | P value | HR (95% CI) | P value |
| Age, years | | | | | | |
| <50 | 12 (29.3) | 2.2 | 1.747 (0.763–4.002) | 0.187 | | |
| 50–60 | 13 (31.7) | 6.5 | 0.809 (0.339–1.929) | 0.632 | | |
| >60 | 16 (39.0) | 4.4 | – | | | |
| Sex | | | | | | |
| Male | 29 (70.7) | 5.6 | 0.834 (0.380–1.829) | 0.651 | | |
| Female | 12 (29.3) | 3.0 | – | | | |
| Smoking | | | | | | |
| No/light | 31 (75.6) | 3.0 | 1.519 (0.655–3.523) | 0.330 | | |
| Heavy | 10 (24.4) | 12.9 | – | | | |
| ECOG | | | | | | |
| 0–1 | 31 (75.6) | 6.3 | 0.414 (0.182–0.939) | 0.035 | 0.602 (0.251–1.441) | 0.254 |
| 2–3 | 10 (24.4) | 2.3 | – | | – | |
| ECM | | | | | | |
| Present | 36 (87.8) | 13.8 | 1.627 (0.562–4.711) | 0.369 | | |
| Absent | 5 (12.2) | 3.4 | – | | | |
| No. of BMs | | | | 0.159 | | |
| <5 | 22 (53.7) | 4.4 | 0.382 (0.142–1.028) | | | |
| 5–10 | 13 (31.7) | 5.6 | 0.458 (0.162–1.298) | | | |
| >10 | 6 (14.6) | 2.8 | – | | | |
| DS-GPA | | | | | | |
| 0–1 | 7 (17.1) | 3.4 | 1.525 (0.506–4.596) | 0.454 | | |
| 1.5–2 | 25 (61.0) | 5.6 | 0.873 (0.364–2.098) | 0.762 | | |
| 2.5–3.0 | 9 (21.9) | 3.2 | – | | | |
| Cerebellum Metastasis | | | | | | |
| Yes | 20 (48.8) | 2.8 | 2.948 (1.326–6.556) | 0.008 | 2.552 (1.128–5.772) | 0.024 |
| No | 21 (51.2) | 13.8 | – | | – | |
| Neurological symptom | | | | | | |
| Yes | 13 (31.7) | 3.0 | 1.259 (0.587–2.696) | 0.554 | | |
| No | 28 (68.3) | 4.4 | – | | | |
| Radiotherapy | | | | | | |
| Yes | 21 (51.2) | 4.4 | 1.181 (0.578–2.416) | 0.648 | | |
| No | 20 (48.8) | 3.0 | – | | | |
| ICI Line | | | | | | |
| 1 | 13 (31.7) | 3.5 | 0.828 (0.388–1.765) | 0.625 | | |
| ≥2 | 28 (68.3) | 3.4 | – | | | |
| Treatment regimen | | | | | | |
| Mono | 16 (39.0) | 2.8 | 1.925 (0.938–3.948) | 0.074 | 1.518 (0.702–3.283) | 0.289 |
| Combination | 25 (61.0) | 6.3 | – | | – | |

Factors with P value <0.1 in univariate analysis were included to multivariate analysis, but "No. of BMs" was excluded causing collinearity with "Cerebellum Metastasis". PFS, progression-free survival; ECOG, Eastern Cooperative Oncology Group; ECM, extracranial metastases; BMs, brain metastases; DS-GPA, diagnosis-specific graded prognostic assessment; ICI, immune checkpoint inhibitor; Mono, monotherapy.

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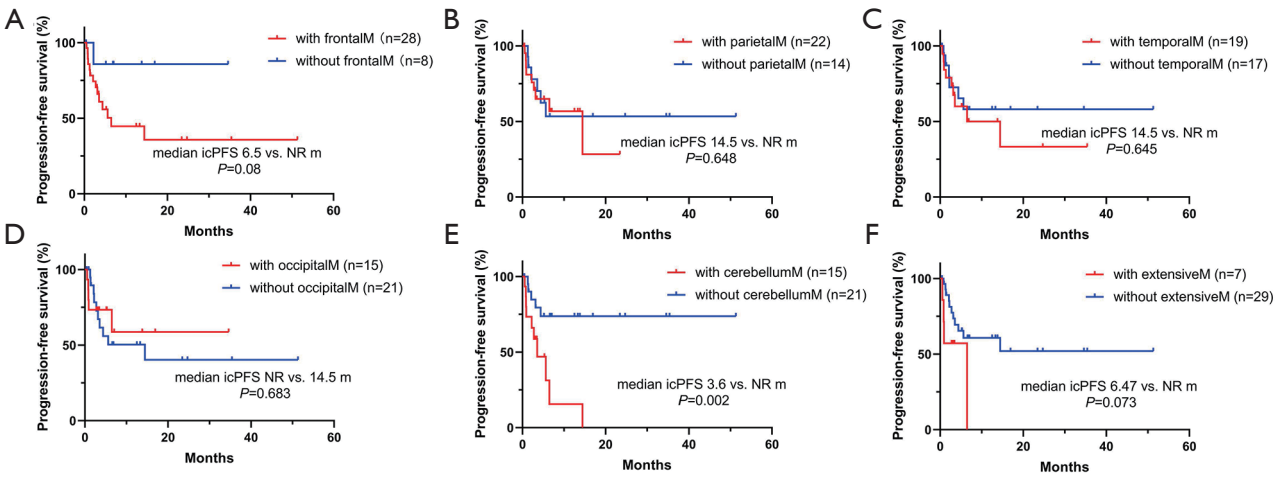


**Figure S4** icPFS comparison between patients with or without different region metastases: frontal lobe (A), parietal lobe (B), temporal lobe (C), occipital lobe (D), cerebellum (E), and concurrent the above five regions (F). icPFS intracranial progression-free survival.

**Table S2** List of target genes predicted from the upregulated miRNAs in patients with cerebellum metastasis, compared with those without

| | | | | | |
|---|---|---|---|---|---|
| *KANSL2* | *BCAN* | *RAB38* | *TSSC4* | *BHLHE40* | *ARHGEF19* |
| *TCTN2* | *AURKA* | *BORCS5* | *GTF3A* | *TMEM250* | *TSEN2* |
| *MYO15A* | *FYCO1* | *COL16A1* | *COL16A1* | *MAEL* | *DPYSL2* |
| *RPP25* | *HIP1R* | *AGBL5* | *TCTN2* | *CFAP99* | *PAPSS1* |
| *RPUSD2* | *ADAMTSL5* | *BLACAT1* | *AKR1E2* | *GOLM1* | |

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