Appendix 1. Radiological characteristics of BMs and clinical characteristics of patients

The MRI radiological characteristics of BMs lesions, including the number of lesions, lesion diameter, intracranial location of onset, lesion enhancement degree, peritumoral edema, necrosis, hemorrhage, skull metastasis, and meningeal metastasis, were analyzed. Additionally, the clinical characteristics of the patients, such as age, gender, underlying diseases, extracranial metastasis, pulmonary surgery, pulmonary lesion location, Karnofsky Performance Status (KPS) score, clinical TNM staging, clinical stage, and serum tumor markers [carcinoembryonic antigen (CEA), neuron-specific enolase (NSE), and cytokeratin-19 fragment (CY211)], were recorded. Comparative analyses of clinical characteristics were conducted at the patient level. All patients enrolled underwent brain MRI examinations. The detailed documentation of the patient recruitment process across the three institutions is presented in Figure S1.

Appendix 2. MRI protocol

We collected the first craniocerebral MRI scans for all enrolled patients, including for the following sequences: axial T1WI, DWI (with a b-value of 1,000 s/mm^2), T2-FLAIR, T2WI, and tri-planar CE-T1WI. Detailed scanning parameters of the MRI sequences are shown in Table S1.

Appendix 3. Seven patterns

Figures S2-S7 are examples of MRI presentation patterns I–VII (DWI-negative plus CE-T1WI-positive, DWI-negative plus T1Gd-Ring, DWI-positive plus CE-T1WI-positive, DWI ring plus T1Gd-positive, DWI-positive plus CE-T1WI ring, DWI ring plus T1Gd ring, and DWI-positive plus CE-T1WI-negative) of SCLC BMs, NSCLC BMs, AD BMs, SCC BMs, EGFR wild-type BMs, and EGFR mutant-type BMs.

Appendix 4. Part I analysis of the clinical characteristics of patients with BMs

As shown in Table S2, the differences between SCLC and NSCLC in terms of supratentorial and infratentorial distribution was significantly different in Center 1 and Center 2 and the overall cohort (P<0.001). In the overall cohort, both SCLC and NSCLC had a higher proportion of BMs in the supratentorial region than in the infratentorial region: for SCLC, 77.9% in the supratentorial region *vs.* 22.1% in the infratentorial region; for NSCLC, 82.5% in the supratentorial region *vs.* 17.5% in the infratentorial region. In the analysis of the supratentorial lesions, the distribution between cortical/subcortical and deep brain locations differed significantly in Center 1 and Center 3 and in the overall cohort (P<0.05). In the overall cohort, the proportion BMs located in the cortical or subcortical regions was higher than that of those located in the deep brain (SCLC: 57.8% cortical or subcortical regions *vs.* 20.1% deep brain; NSCLC: 67.9% cortical or subcortical regions *vs.* 14.7% deep brain). SCLC and NSCLC differed significantly in terms of cortical or subcortical BMs in Center 1 and the overall cohort (P<0.05). In the overall cohort, NSCLC, as compared to SCLC, had a higher proportion of BMs in the frontal lobe (27.9% *vs.* 24.6%) and parietal lobe (16.0% *vs.* 14.5%). NSCLC had the lowest proportion of BMs in the temporal lobe (10.7%), and SCLC had the lowest proportion of BMs in the occipital lobe (8.2%).In the overall cohort, NSCLC had a higher proportion of BMs in the centrum semiovale than did SCLC (4.0% *vs.* 3.6%), while SCLC had a higher proportion of BMs around the ventricles than did NSCLC (9.1% *vs.* 5.8%). In the analysis of the infratentorial region, there was no significant difference between SCLC and NSCLC in terms of cerebellar and brainstem BM distribution in the three centers or the overall cohort (P>0.05). In the overall cohort, the proportion of BMs in the cerebellum was higher than that of those in the brainstem [SCLC: 20.1% (cerebellum) *vs.* 2.0% (brainstem); NSCLC: 15.6% (cerebellum) *vs.* 1.9% (brainstem)].

As shown in Table S3, compared to SCLC, the NSCLC group had a higher proportion of females, nonsmokers, and lung cancer lesions located in the right lobe of the lung. A greater portion of patients with NSCLC had meningeal metastasis and underwent lung cancer surgery. Regarding the TNM staging of lung cancer, the SCLC group a higher proportion of patients at an advanced T stage (T3+T4 was more common that T1+T2), while the NSCLC group had a higher proportion of patients at an advance N stage (N2+N3 was more common than N0+N1). However, only Center 2 showed a statistically significant difference between SCLC and NSCLC in terms of M stage (P<0.001). SCLC tended to have a high expression of

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Ki-67 (Ki-67 >50%). NSCLC had higher CEA levels, higher CY211 levels, and lower NSE levels as compared to NSCLC. The other characteristics, including basic disease, KPS score, extracranial metastases, clinical stage, age, and cranial bone metastasis, were not significantly different between SCLC and NSCLC in the three centers or the overall cohort (all P values >0.05).

Appendix 5. Part II analysis of the clinical characteristics of patients with BMs

As shown in Table S4, AD and SCC were significantly different in terms of supratentorial and infratentorial BM distribution in Center 1 and the overall cohort (P<0.05). Both AD and SCC a higher proportion of BMs in the supratentorial region than in the infratentorial region (AD: 82.0% *vs.* 18.0%; SCC: 91.4% *vs.* 8.6%). In the analysis of the supratentorial region, AD and SCC did not differ significantly in terms of BM cortical or subcortical brain distribution in the three centers or the overall cohort (all P values >0.05). In the overall cohort, the proportion BMs in the cortical or subcortical regions was higher than that of BMs in the deep brain (AD: 67.4% *vs.* 14.5%; SCC: 72.3% *vs.* 18.3%). There was no difference between AD and SCC in terms of cortical or subcortical distribution in the three centers or the overall cohort (all P values >0.05). In the overall cohort, both AD and SCC had the highest proportion of BMs in the frontal lobe (27.8% *vs.* 30.5%), with similar proportions in the parietal (15.9% *vs.* 16.6%), temporal (10.7% *vs.* 10.0%), and occipital (13.1% *vs.* 15.2%) lobes. The proportion of deep brain region BMs differed significantly between AD and SCC in Center 1 (P=0.005) and the overall cohort (P=0.008). In the overall cohort, SCC, compared to AD, had a higher proportion of BMs in the centrum semiovale (7.3% *vs.* 3.9%) and periventricular areas (8.0% *vs.* 5.7%). In the analysis of the infratentorial region, there was no statistical difference between AD and SCC in the three centers or the overall cohort (all P value >0.05). In the overall cohort, both AD and SCC a higher proportion of BMs in the cerebellum (16.0% *vs.* 2.0%) than in the brainstem (9.0% *vs.* 0.4%).

As shown in Table S5, the AD group had a higher proportion of females and nonsmokers than did the SCC group and a slightly lower mean age. Regarding the TNM staging of lung cancer, the SCC group had a higher proportion of patients with an advanced T stage (T3+T4 was more common than T1+T2), while the AD group had a higher proportion of patents with an advanced M stage (M1c2 was more common than M1b and M1c1). For the clinical stage, patients with AD, as compared to those with SCC, were more likely to be stage IVB. Meanwhile, those with SCC were more likely to have a high Ki-67 expression (Ki-67 >50%). For common gene mutation types in NSCLC, including EGFR, anaplastic lymphoma kinase (ALK), Kirsten rat sarcoma viral oncogene (KRAS), ROS proto-oncogene 1 (ROS1), tumor protein P53 (TP53), MET proto-oncogene (MET), b-raf proto-oncogene (BRAF), and no gene mutation, the AD and SCC groups only differed significantly in Center 3 (P=0.023). Moreover, patients with AD were more likely to have the EGFR-mutant type. However, in terms of specific EGFR mutant-type (i.e., 19 exon, 21 exon, and 18/20 exon mutations), no significant difference was observed in the three centers or the overall cohort (all P values >0.05). Regarding serum tumor markers, the AD group had higher CEA expression, whereas the SCC group had higher CY211 expression. Other characteristics, including basic disease, KPS score, extracranial metastases, location of lung cancer, lung surgery, PD-L1 expression, NSE, meningeal metastasis, and cranial bone metastasis, were not significantly different between AD and SCC in any of the cohorts (all P values >0.05).

Appendix 6. Part II analysis of the clinical characteristics of patients with BMs

As shown in Table S6, the EGFR wild type and mutant types differed significantly in terms of supratentorial and infratentorial distribution in Center 2 and the overall cohort (P<0.05). Both the wild and mutant types had a higher proportion of BMs in the supratentorial region (81.1% *vs.* 18.9%) than in the infratentorial region (82.2% *vs.* 17.8%). In the supratentorial region, the wild and mutant types did not differ significantly in terms of cortical/subcortical and deep brain BM distribution in the three centers or the overall cohort (all P values >0.05). In the overall cohort, the proportion of BMs in the cortical/ subcortical regions was higher than that of those in the deep brain (wild type: 63.6% (cortical/ subcortical regions) *vs.* 17.4% (deep brain); mutant type: 68.2% (cortical/ subcortical regions) *vs.* 14.0% (deep brain)). The wild and mutant types did not differ significantly in terms of BM distribution in the cortical and subcortical regions in the three centers or the overall cohort (all P values >0.05). In the overall cohort, both the wild and mutant types had the highest proportion of BMs in the frontal lobe (25.0% *vs.* 27.0%), with little difference in the proportion of BMs in the parietal (16.0% *vs.* 15.7%), temporal (10.6% *vs.* 11.0%), and occipital lobes (12.1% *vs.* 13.5%). The wild and mutant types differed significantly in terms of BMs

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in the deep brain region in Center 1 (P=0.005) and the overall cohort (P=0.008). In the overall cohort, the wild type had a higher proportion of BMs in the periventricular area than did the mutant type (8.2% *vs.* 4.8%), but these groups had similar proportions of BMs in the centrum semiovale (4.1% *vs.* 4.3%). In the analysis of the infratentorial region, the wild and mutant types did not differ significantly in terms of BM distribution in the cerebellum and brainstem in the three centers or the overall cohort (all P>0.05). In the overall cohort, the proportion of BMs in the cerebellum was higher than that of those in the brainstem (wild type: 17.3% *vs.* 1.7%; mutant type: 15.7% *vs.* 2.1%).

As shown in Table S7, the mutant-type group had a higher proportion of males and nonsmokers. Regarding TNM staging of lung cancer, the wild-type group had a more advanced T stage (T3+T4 more common than T1+T2). In terms N staging, the wild- and mutant-type groups only differed significantly in Center 2 (P=0.043). In the analysis of pathological subtypes, the mutant-type group had a higher proportion of AD and meningeal metastasis. Regarding serum tumor markers, the mutant-type group had higher CEA. Other characteristics, including basic disease, KPS score, extracranial metastases, location of lung cancer, lung surgery, M staging, clinical staging, Ki-67 expression, PD-L1 expression, NSE, CY211, and cranial bone metastasis, did not differ significantly between the wild-type and mutant-type groups in the three centers or the overall cohort (all P values >0.05).

Appendix 7. Part II analysis of the clinical characteristics of patients with BMs

In our study, serum tumor markers demonstrated a close correlation with the histological subtypes of lung cancer. As a specific marker for neuroendocrine tumors, NSE expression is notably elevated in patients with SCLC, with particularly pronounced increases observed in patients with intermediate- and advanced-stage SCLC (1). This finding is consistent with our research results, with the NSE expression level in patients with SCLC being significantly higher than that in NSCLC (32.36 *vs.* 18.83 ng/mL; P<0.001). CEA and CYFRA21-1 are the most sensitive tumor markers in NSCLC. In our study, CEA expression was higher in AD than in SCC (14.50 *vs.* 4.90 ng/mL; P<0.001), while CYFRA21-1 expression was higher in SCC than in AD (SCC: 7.80 ng/mL; AD: 5.42 ng/mL, P=0.007). These findings are in agreement with reports by Liu *et al.* and the existing literature (2). Ki-67 is the most widely used marker for assessing cell proliferation, and its expression is correlated with the development, metastasis, and prognosis of lung cancer (3). In our study, the high expression of Ki-67 (>50%) in both SCLC and SCC further confirmed the more aggressive nature of SCLC compared to AD. This finding further substantiates the consistency between our research results and clinical observations. However, neither serum tumor markers nor the expression levels of Ki-67 showed significant differences between the EGFR wild-type and mutant-type groups. Additionally, in our study, we observed that EGFR-positive patients were predominantly male, which contrasts with the findings of Marchetti *et al.* (4), who reported that EGFR mutations are more likely to occur in females. This discrepancy may be attributed to sample biases and differences in the number of patients analyzed in our study. Meanwhile, regarding leptomeningeal metastases, although our study indicated a higher likelihood of leptomeningeal involvement in NSCLC than in SCLC, this evidence is not definitive due to the geographical limitations and sample size constraints.

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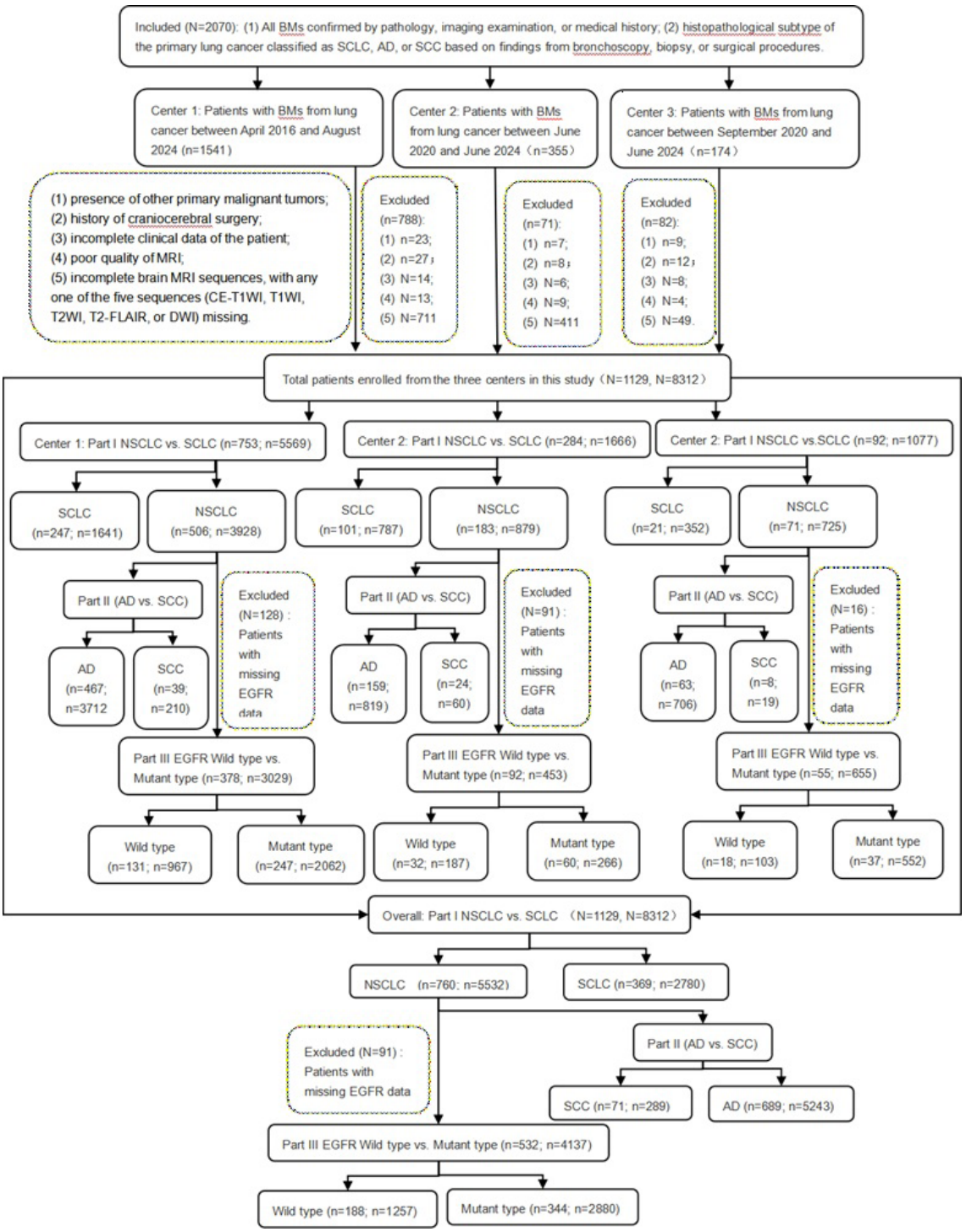

Figure S1 The flowchart of patient inclusion in the retrospective study. N, number of patients; n, number of lesions. If there are two values in parentheses, they are presented as (N/n=number of patients; N/n=number of lesions); If there is only one value in parentheses, it represents (n = number of patients). AD, adenocarcinoma; BM, brain metastasis; CE-T1WI, contrast-enhanced T1-weighted imaging; DWI, diffusion-weighted imaging; EGFR, epidermal growth factor receptor; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; SCC, squamous cell cancer; SCLC, small-cell lung cancer; T1WI, T1-weighted imaging; T2-FLAIR, T2-fluid-attenuated inversion recovery; T2WI, T2-weighted imaging.

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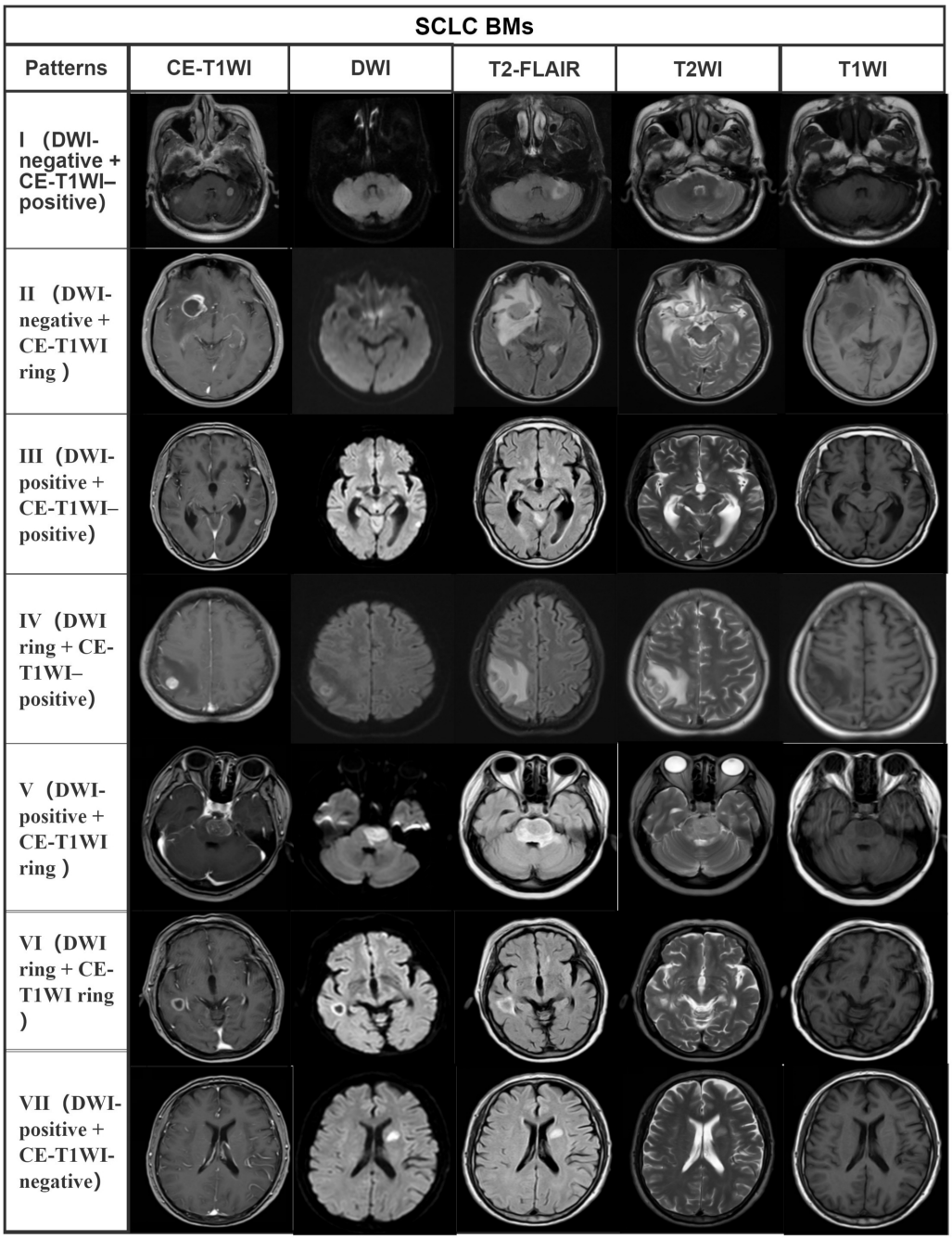

Figure S2 MRI presentation patterns I–VII for SCLC BM cases. Pattern I: a 57-year-old male with multiple intracranial lesions, one of which was located in the left cerebellar hemisphere. Pattern II: a 67-year-old male with four intracranial lesions, one of which was located in the right frontal lobe. Pattern III: a 72-year-old male with multiple intracranial lesions, one of which was located in the left temporal lobe. Pattern IV: a 53-year-old female with one intracranial lesion located in the right parietal lobe. Pattern V: a 52-year-old female with four intracranial lesions, one of which was located in the right temporal lobe. Pattern VI: a 72-year-old female with four intracranial lesions, one of which is located in the right temporal lobe. Pattern VII: a 57-year-old male with three intracranial lesions, one of which was located adjacent to the left lateral ventricle. BM, brain metastasis; CE-T1WI, contrast-enhanced T1-weighted imaging; DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; SCLC, small cell lung cancer; T1WI, T1-weighted imaging; T2-FLAIR, T2-fluid-attenuated inversion recovery; T2WI, T2-weighted imaging.

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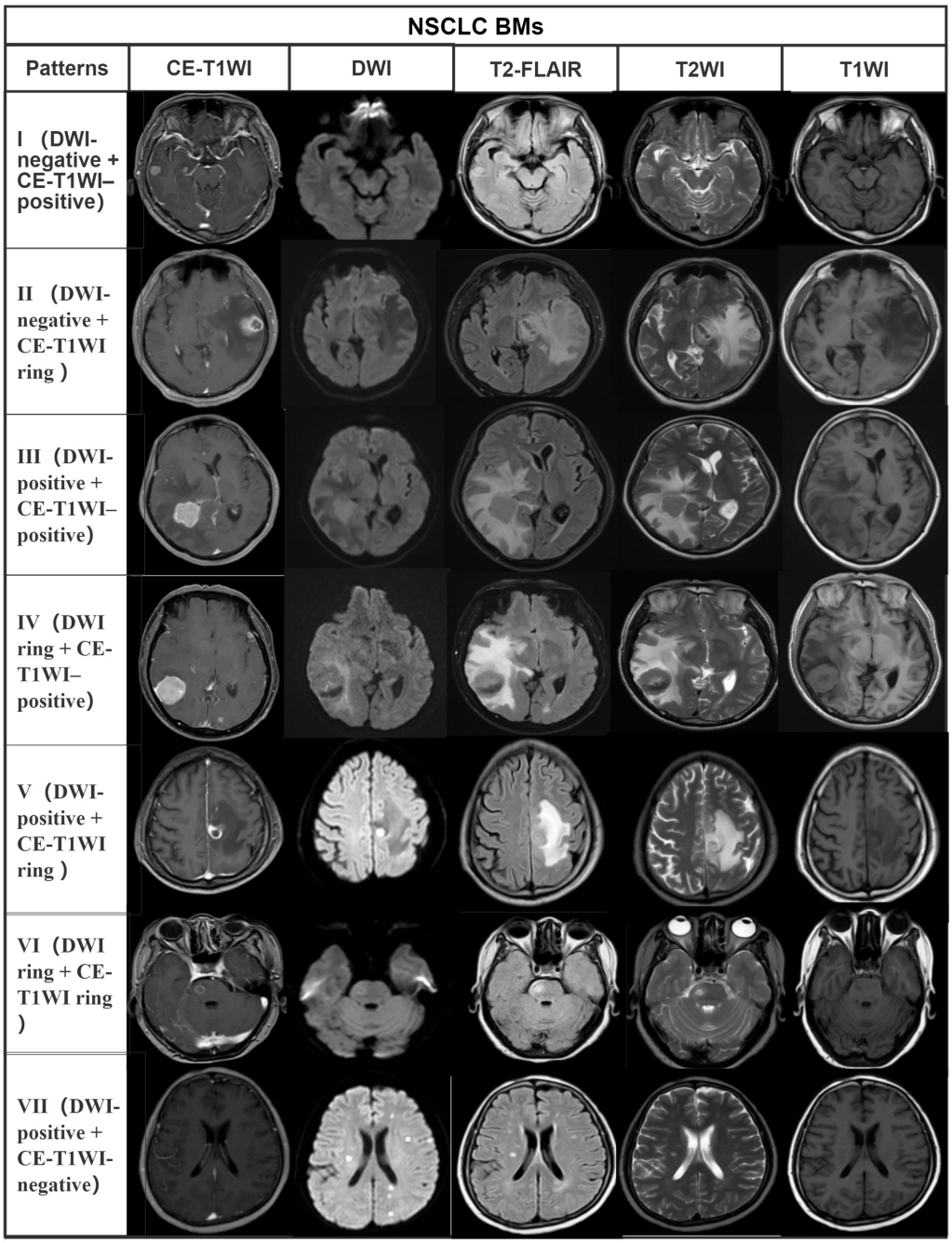

Figure S3 MRI presentation patterns I–VII for NSCLC BM cases. Pattern I: a 51-year-old male with one intracranial lesion located in the right temporal lobe. Pattern II: a 60-year-old male with four intracranial lesions, one of which was located in the left temporal lobe. Pattern III: a 62-year-old female with one intracranial lesion located adjacent to the posterior horn of the right lateral ventricle. Pattern IV: a 52-year-old male with two intracranial lesions, one of which was located in the right temporo-occipital lobe. Pattern V: a 61-year-old male with one intracranial lesion located in the left parietal lobe. Pattern VI: a 56-year-old female with three intracranial lesions, one of which was located on the right side of the pons. Pattern VII: a 55-year-old female with multiple intracranial lesions, several of which were located around the bilateral lateral ventricles. BM, brain metastasis; CE-T1WI, contrast-enhanced T1-weighted imaging; DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; T1WI, T1-weighted imaging; T2-FLAIR, T2-fluid-attenuated inversion recovery; T2WI, T2-weighted imaging.

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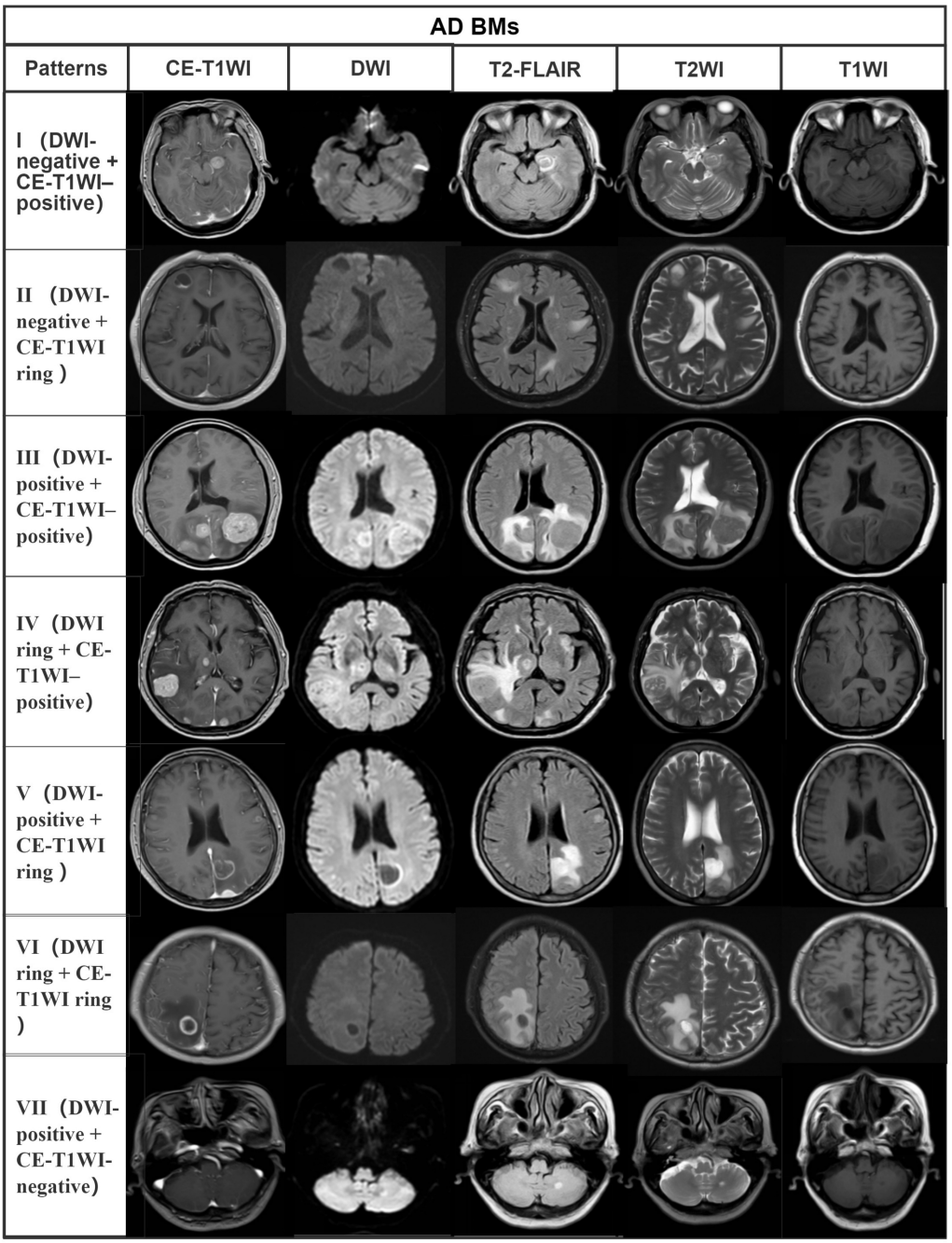

Figure S4 MRI presentation patterns I–VII of AD BM cases. Pattern I: a 47-year-old female with multiple intracranial lesions located in the left cerebellar hemisphere. Pattern II: a 70-year-old male with eight intracranial lesions, one of which was located in the right frontal lobe. Pattern III: a 47-year-old female with four intracranial lesions, two of which were located in the bilateral occipital lobes. Pattern IV: a 72-year-old male with multiple intracranial lesions, one of which was located in the right thalamus. Pattern V: a 66-year-old female with multiple intracranial lesions, one of which was located in the left parietal lobe. Pattern VI: a 40-year-old male with two intracranial lesions, one of which was located in the right parietal lobe. Pattern VII: a 76-year-old female with one intracranial lesion located in the left cerebellar hemisphere. AD, adenocarcinoma; BM, brain metastasis; CE-T1WI, contrast-enhanced T1-weighted imaging; DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; T1WI, T1-weighted imaging; T2-FLAIR, T2-fluid-attenuated inversion recovery; T2WI, T2-weighted imaging.

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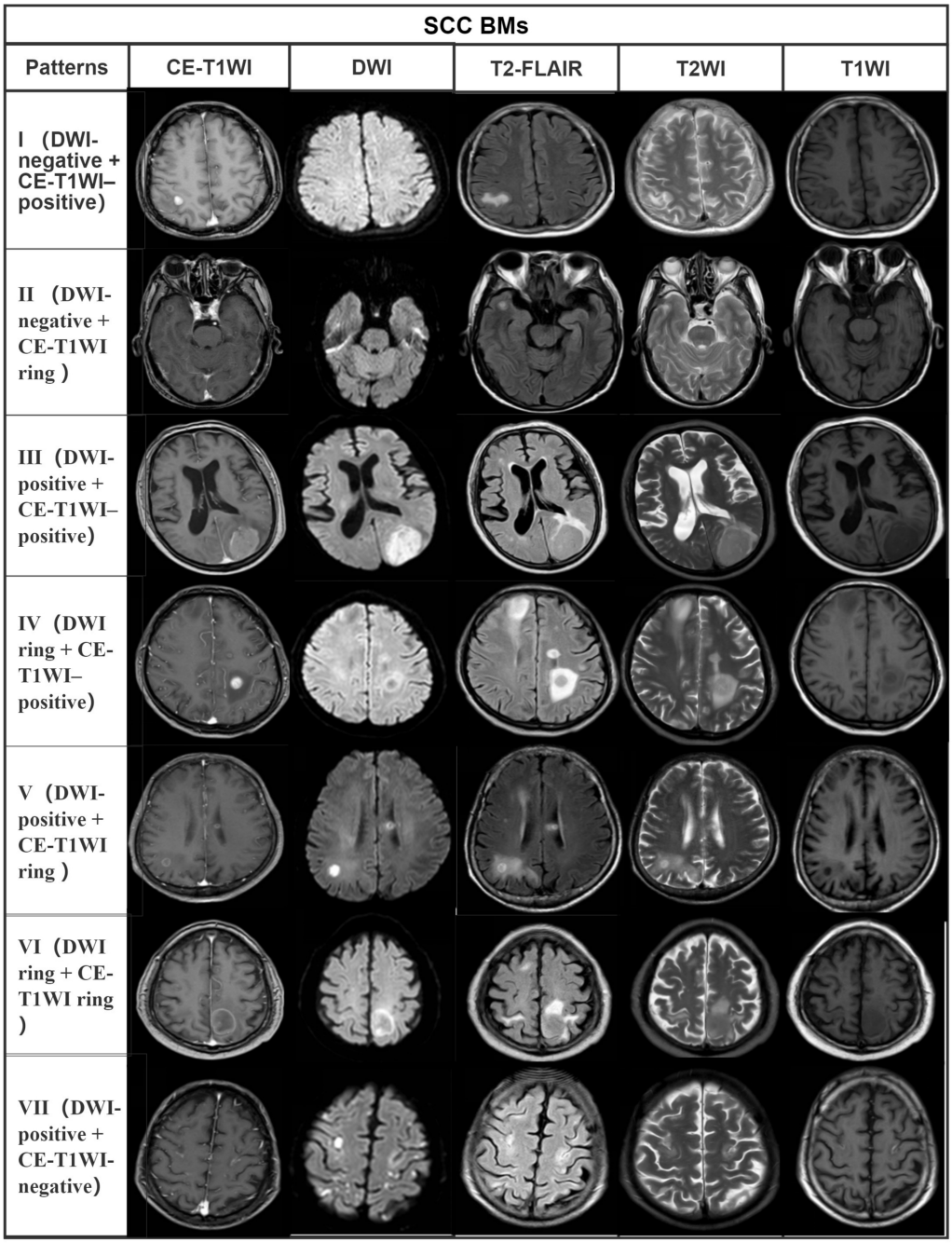

Figure S5 MRI presentation patterns I–VII for SCC BM cases. Pattern I: a 54-year-old female with two intracranial lesions, one of which was located in the right parietal lobe. Pattern II: a 63-year-old male with one intracranial lesion located in the right temporal lobe. Pattern III: a 70-year-old male with two intracranial lesions, one of which was located in the left occipital lobe. Pattern IV: a 49-year-old male with multiple intracranial lesions, one of which was located in the left parieto-occipital lobe. Pattern V: a 71-year-old male with multiple intracranial lesions, one of which was located in the right parietal lobe. Pattern VI: a 66-year-old male with multiple intracranial lesions, one of which was located in the left parietal lobe. Pattern VII: a 59-year-old male with multiple intracranial lesions, one of which was located in the right parietal lobe. BM, brain metastasis; CE-T1WI, contrast-enhanced T1-weighted imaging; DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; SCC, squamous cell cancer; T1WI, T1-weighted imaging; T2-FLAIR, T2-fluid-attenuated inversion recovery; T2WI, T2-weighted imaging.

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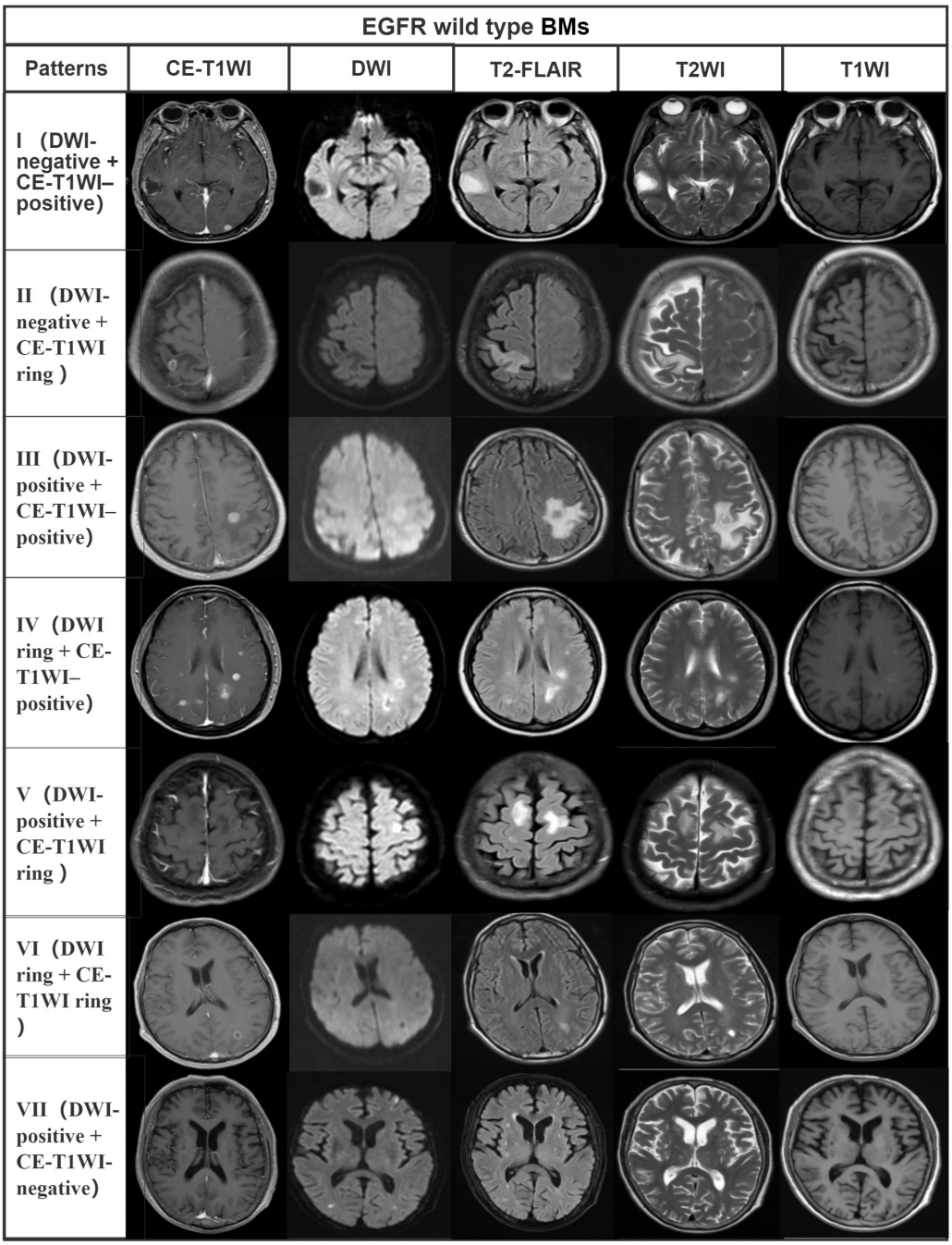

Figure S6 MRI presentation patterns I–VII for BMs in EGFR wild-type cases. Pattern I: a 64-year-old female with multiple intracranial lesions located in the right occipital lobe. Pattern II: a 60-year-old male with four intracranial lesions, one of which was located in the right parietal lobe. Pattern III: a 66-year-old male with seven intracranial lesions, one of which was located in the left parietal lobe. Pattern IV: a 41-year-old female with multiple intracranial lesions, one of which was located in the left corona radiata. Pattern V: a 60-year-old male with multiple intracranial lesions, one of which was located in the left frontal lobe. Pattern VI: a 66-year-old male with seven intracranial lesions, one of which was located in the left occipital lobe. Pattern VII: a 69-year-old male with multiple intracranial lesions, one of which was located in the right occipital lobe. BM, brain metastasis; CE-T1WI, contrast-enhanced T1-weighted imaging; DWI, diffusion-weighted imaging; EGFR, epidermal growth factor receptor; MRI, magnetic resonance imaging; T1WI, T1-weighted imaging; T2-FLAIR, T2-fluid-attenuated inversion recovery; T2WI, T2-weighted imaging.

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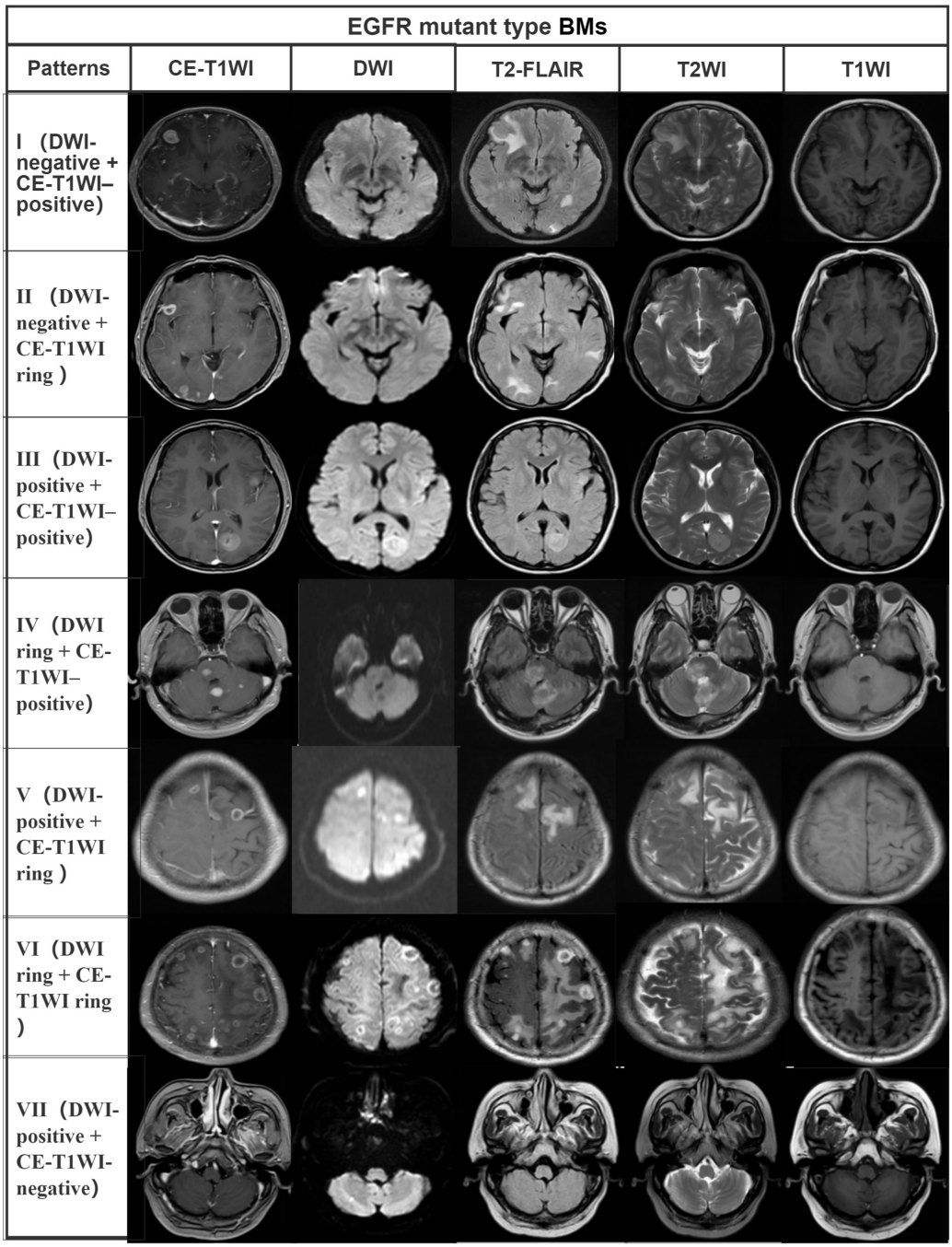

Figure S7 MRI presentation patterns I–VII for BMs in EGFR mutant-type cases. Pattern I: a 52-year-old male with multiple intracranial lesions, one of which was located in the right frontal lobe. Pattern II: a 70-year-old female with multiple intracranial lesions, one of which was located in the right frontal–temporal junction area. Pattern III: a 47-year-old female with eight intracranial lesions, one of which was located in the left occipital lobe. Pattern IV: a 38-year-old male with multiple intracranial lesions, one of which was located in the cerebellar vermis. Pattern V: a 68-year-old male with multiple intracranial lesions, three of which were located in the bilateral frontal lobes. Pattern VI: a 65-year-old female with multiple intracranial lesions, several of which were located in the bilateral frontal-parietal lobes. Pattern VII: a 51-year-old male with seven intracranial lesions, one of which was located in the right cerebellar hemisphere. BM, brain metastasis; CE-T1WI, contrast-enhanced T1-weighted imaging; DWI, diffusion-weighted imaging; EGFR, epidermal growth factor receptor; MRI, magnetic resonance imaging; T1WI, T1-weighted imaging; T2-FLAIR, T2-fluid-attenuated inversion recovery; T2WI, T2-weighted imaging.

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Table S1 Imaging parameters of different MR scanners in different centers

Number	Center	MR scanner and magnetic field strength	CE-T1WI (TR/TE)	DWI (TR/TE)	T2-FLAIR (TR/TE)	T2WI (TR/TE)	T1WI (TR/TE)
1	1	GE Discovery MR750; 3.0T	2,146/21	2,454/66	6,500/144	7,444/96	2,088/26
2	1	United Imaging uMR 588; 1.5 T	11/4	4,079/107	8,000/138	4,000/99	1,873/10
3	1	Philips Achieva; 1.5 T	167/2	3,374/82	6,000/130	2,697/100	167/2
4	1	Siemens Avanto; 1.5 T	234/5	3,000/87	8,000/109	4,091/95	214/5
5	1	Siemens Amira; 1.5 T	339/4	4,000/85	8,000/84	2,430/106	1,640/10
6	1	Siemens Area; 3.0T	192/5	5,300/106	7,500/82	4,000/93	2,000/12
7	2	Philips Ingenia LS; 3.0T	153/2	2,498/89	9,000/130	3,746/100	461/14
8	2	Philips Achieva; 1.5T	120/2	2,467/95	7,000/125	2,139/80	2,000/20
9	2	Philips Multiva; 3.0T	123/2	2,657/98	6,000/100	3,895/100	487/15
10	3	United Imaging uMR 780; 3.0T	7/3	2,000/76	5,000/408	4,075/100	220/3
11	3	Siemens Skyra; 3.0T	1,700/2	4,100/64	9,000/96	4,500/103	150/2
12	3	Siemens Avanto; 1.5T	1,340/3	3,500/87	8,000/108	3,500/94	185/5
13	3	Siemens MAGNETOM Vida; 3.0T	1,500/3	3,870/63	6,000/96	4,000/107	220/2
14	3	Philips Ingenia CX; 3.0T	5/2	2,119/66	11,000/125	3,000/113	6/3

CE-T1WI, contrast-enhanced T1-weighted imaging; DWI, diffusion-weighted imaging; MR, magnetic resonance; TE, echo time; TR, repetition time; T1WI, T1-weighted imaging; T2-FLAIR, T2-fluid-attenuated inversion recovery; T2WI, T2-weighted imaging.

Table S2 Lesion-level MRI radiological characteristics in Part I

Characteristic	Center 1 (n=5,569)			Center 2 (n=1,666)			Center 3 (n=1,077)			Overall (N=8,312)		
	SCLC	NSCLC	P value	SCLC	NSCLC	P value	SCLC	NSCLC	P value	SCLC	NSCLC	P value
Location of BMs			<0.001*			<0.001*			0.972			<0.001*
Supratentorial area	1,250 (76.2)	3,241 (82.5)	0.029*	597 (75.9)	735 (83.6)	0.076	318 (90.3)	589 (81.2)	<0.001*	2,165 (77.9)	4,565 (82.5)	<0.001*
Cortical or subcortical	936 (57.0)	2,623 (66.8)	0.005*	445 (56.5)	600 (68.3)	0.854	226 (64.2)	531 (73.2)	0.536	1,607 (57.8)	3,754 (67.9)	0.013*
Frontal lobe	408 (24.9)	1,064 (27.1)		192 (24.4)	259 (39.5)		84 (23.9)	220 (30.3)		684 (24.6)	1,543 (27.9)	
Parietal lobe	237 (14.4)	635 (16.2)		106 (13.5)	148 (16.8)		61 (17.3)	100 (13.8)		404 (14.5)	883 (16.0)	
Temporal lobe	162 (9.9)	397 (10.1)		76 (9.7)	102 (11.6)		52 (14.8)	91 (12.6)		290 (10.4)	590 (10.7)	
Occipital lobe	129 (7.9)	527 (13.4)		71 (9.0)	91 (10.4)		29 (8.2)	120 (16.6)		229 (8.2)	738 (13.3)	
Deep brain	314 (19.1)	618 (15.7)	0.019*	152 (19.3)	135 (15.4)	0.410	92 (26.1)	58 (8.0)	0.035*	558 (20.1)	811 (14.7)	0.002*
Centrum semiovale	63 (3.8)	197 (5.0)		32 (4.1)	14 (1.6)		5 (1.4)	12 (1.7)		100 (3.6)	223 (4.0)	
Periventricular	142 (8.7)	217 (5.5)		74 (9.4)	84 (9.6)		38 (10.8)	22 (3.0)		254 (9.1)	323 (5.8)	
Intraventricular	12 (0.7)	9 (0.2)		5 (0.6)	3 (0.3)		1 (0.3)	0		18 (0.7)	12 (0.2)	
Callosum	16 (1.0)	32 (0.8)		5 (0.6)	8 (0.9)		4 (1.1)	5 (0.7)		25 (0.9)	45 (0.8)	
Thalamus	28 (1.7)	72 (1.8)		12 (1.5)	6 (0.7)		19 (5.4)	7 (1.0)		59 (2.1)	85 (1.5)	
Basal ganglia region	53 (3.2)	91 (2.3)		24 (3.1)	20 (2.3)		25 (7.1)	12 (1.7)		102 (3.7)	123 (2.2)	
Infratentorial area	391 (23.8)	687 (17.5)	0.190	190 (24.1)	144 (16.4)	0.269	34 (9.7)	136 (18.8)	0.642	615 (22.1)	967 (17.5)	0.289
Cerebellum	355 (21.6)	606 (15.4)		175 (22.2)	137 (15.6)		29 (8.2)	120 (16.6)		559 (20.1)	863 (15.6)	
Brainstem	36 (2.2)	81 (2.1)		15 (1.9)	7 (0.8)		5 (1.4)	16 (2.2)		56 (2.0)	104 (1.9)	

Categorical variables are described as n (%). For qualitative variables, the Pearson χ^2 test or Fisher exact test was used to determine whether there were statistically significant differences. Due to the presence of missing values, the sum of case numbers in each group may not equal the total number of cases; due to rounding, the sum of percentages may not equal 100%. The P value represents the analysis of the significance of differences within the data groups from the three centers and the overall dataset. A P value below 0.05 is considered statistically significant. *, P<0.05. Center 1: Affiliated Hospital of Hebei University; Center 2: Baoding First Central Hospital; Center 3: The Fourth Affiliated Hospital of Hebei Medical University. BM, brain metastasis; MRI, magnetic resonance imaging; SCLC, small-cell lung cancer; NSCLC, non-small cell lung cancer.

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Table S3 Patient-level clinical characteristics of patients with BM in Part I

Characteristic	Center 1 (n=753)			Center 2 (n=284)			Center 3 (n=92)			Overall (N=1,129)		
	SCLC	NSCLC	P value	SCLC	NSCLC	P value	SCLC	NSCLC	P value	SCLC	NSCLC	P value
Number of patients	247	506		101	183		21	71		369	760	
Gender			<0.001*			<0.001*			0.008*			<0.001*
Male	183 (74.1)	153 (30.2)		85 (84.2)	104 (56.8)		19 (90.5)	42 (59.2)		287 (77.8)	299 (39.3)	
Female	64 (25.9)	353 (69.8)		16 (15.8)	79 (43.2)		2 (9.5)	29 (40.8)		82 (22.2)	461 (60.7)	
Tobacco use			<0.001*			<0.001*			0.581			<0.001*
Non-smokers	85 (34.4)	286 (56.5)		27 (26.7)	107 (58.5)		11 (52.4)	42 (59.2)		123 (33.3)	435 (57.2)	
Smoker	162 (65.6)	220 (43.5)		74 (73.3)	76 (41.5)		10 (47.6)	29 (40.8)		246 (66.7)	325 (42.8)	
Basic disease[†]						0.205			0.190			0.447
No	127 (51.4)	269 (53.2)	0.753	54 (53.5)	112 (61.2)		16 (76.2)	43 (60.6)		197 (53.4)	424 (55.8)	
Yes	120 (48.6)	237 (46.8)		47 (46.5)	71 (38.8)		5 (23.8)	28 (39.4)		172 (46.6)	336 (44.2)	
KPS score			0.551			0.982			0.717			0.990
≤70	66 (26.7)	124 (24.5)		6 (42.9)	38 (43.2)		11 (42.4)	34 (47.9)		83 (29.4)	196 (29.5)	
>70	181 (73.3)	382 (75.5)		8 (57.1)	50 (56.8)		10 (47.6)	37 (52.1)		199 (70.6)	469 (70.5)	
Extracranial metastases			0.104			0.740			0.717			0.272
No	106 (42.9)	186 (36.8)		57 (56.4)	107 (58.5)		10 (47.6)	37 (52.1)		173 (46.9)	330 (43.4)	
Yes	141 (57.1)	320 (63.2)		44 (43.6)	76 (41.5)		11 (42.4)	34 (47.9)		196 (53.1)	430 (56.7)	
Location of LC			0.010*			<0.001*			0.770			0.001*
Left lung	112 (45.3)	221 (43.7)		67 (66.3)	46 (25.1)		9 (42.9)	33 (46.5)		188 (50.9)	300 (39.5)	
Right lung	134 (54.3)	283 (55.9)		34 (33.7)	137 (74.9)		12 (57.1)	38 (53.5)		180 (48.8)	458 (60.3)	
Others	1 (0.4)	2 (0.4)		0	0		0	0		1 (0.3)	2 (0.3)	
Lung surgery			<0.001*			0.043*			0.378			<0.001*
No	241 (97.6)	415 (82.0)		97 (96.0)	163 (89.1)		20 (95.2)	63 (88.7)		358 (97.0)	641 (84.3)	
Yes	6 (2.4)	91 (18.0)		4 (4.0)	20 (10.9)		1 (4.8)	8 (11.3)		11 (3.0)	119 (15.7)	
T staging of TNM			<0.001*			0.807			0.313			<0.001*
T1+T2	55 (35.9)	194 (57.6)		3 (17.6)	19 (20.2)		2 (33.3)	20 (55.6)		60 (34.1)	233 (49.9)	
T3+T4	98 (64.1)	143 (42.4)		14 (82.4)	75 (79.8)		4 (66.7)	16 (44.4)		116 (65.9)	234 (50.1)	
N staging of TNM			<0.001*			0.422			0.105			0.045*
N0+N1	19 (12.4)	92 (27.2)		57 (85.1)	107 (80.5)		0	10 (28.6)		76 (33.5)	209 (41.3)	
N2+N3	134 (87.6)	246 (72.8)		10 (14.9)	26 (19.5)		7 (100.0)	25 (71.4)		151 (66.5)	297 (58.7)	
M staging of NM			0.217			<0.001*			0.531			0.205
M1b	45 (18.2)	86 (17.0)		50 (49.5)	47 (25.7)		10 (47.6)	37 (52.1)		112 (30.4)	230 (30.3)	
M1c1	61 (24.7)	100 (19.8)		7 (6.9)	60 (32.8)		1 (4.8)	8 (11.3)		106 (28.7)	184 (24.2)	
M1c2	141 (57.1)	320 (63.2)		44 (43.6)	76 (41.5)		10 (47.6)	26 (36.6)		151 (40.9)	346 (45.5)	
Clinical staging			0.678			0.740			0.717			0.818
IVA	45 (18.2)	86 (17.0)		44 (43.6)	76 (41.5)		10 (47.6)	37 (52.1)		99 (26.8)	199 (26.2)	
IVB	202 (81.8)	420 (83.0)		57 (56.4)	107 (58.5)		11 (52.4)	34 (47.9)		270 (73.2)	561 (73.8)	
Ki-67			<0.001*			<0.001*			<0.001*			<0.001*
<25%	3 (1.6)	41 (30.6)		0	29 (24.8)		0	7 (21.9)		3 (1.1)	77 (27.2)	
25–50%	3 (1.6)	38 (28.4)		1 (1.5)	31 (26.5)		1 (5.6)	14 (43.8)		5 (1.9)	83 (29.3)	
>50%	178 (96.7)	55 (41.0)		66 (98.5)	57 (48.7)		17 (94.4)	11 (34.4)		261 (97.0)	123 (43.5)	
Age (years)	62.7±9.0	62.1±9.7	0.290	62.6±8.7	63.6±9.3	0.206	61.0±8.3	59.4±8.2	0.542	62.5±8.8	62.2±9.5	0.528
CEA (ng/mL)	4.25 (2.40, 10.50)	13.85 (4.06, 74.13)	<0.001*	3.79 (2.53, 7.96)	11.5 (3.72, 65.45)	<0.001*	5.62 (3.34, 1.08)	11.51 (3.40.61.29)	0.034*	4.10 (2.51, 9.25)	13.10 (3.95, 70.08)	<0.001*
NSE (ng/mL)	39.55 (16.40, 86.40)	17.50 (13.40.27.85)	<0.001*	28.84 (18.57, 49.96)	22.70 (17.87, 32.67)	0.003*	23.60 (17.19, 50.50)	16.20 (14.32, 22.54)	0.002*	32.36 (16.92, 73.45)	18.83 (14.33, 29)	<0.001*
CY211 (ng/mL)	3.80 (2.26, 10.19)	5.76 (2.88, 13.18)	<0.001*	2.83 (1.95, 5.63)	5.59 (3.04, 12.38)	<0.001*	3.15 (2.42, 4.23)	4.48 (2.56, 11.84)	0.045*	3.37 (2.15, 8.08)	5.57 (2.88, 12.73)	<0.001*
Meningeal metastasis			0.034*			0.669			0.266			0.024*
No	242 (98.0)	479 (94.7)		100 (99.0)	182 (99.5)		21 (100.0)	67 (94.4)		363 (98.4)	731 (96.2)	
Yes	5 (2.0)	27 (5.3)		1 (1.0)	1 (0.5)		0	4 (5.6)		6 (1.6)	29 (3.8)	
Cranial bone metastasis			0.166			0.575			0.168			0.064
No	242 (98.0)	486 (96.0)		97 (96.0)	173 (94.5)		21 (100.0)	65 (91.5)		360 (97.6)	724 (95.3)	
Yes	5 (2.0)	20 (4.0)		4 (4.0)	10 (5.5)		0	6 (8.5)		9 (2.4)	36 (4.7)	

Categorical variables are described as N (%). Continuous variables are presented as the median (Q1, Q3) or as the mean (standard deviation), denoted as mean ± SD. For continuous variables, the Student *t* test or Mann-Whitney U test was used to assess statistical significance; for qualitative variables, the Pearson χ^2 test or Fisher exact test was employed to determine if there were statistically significant differences. Due to the presence of missing values, the sum of case numbers in each group may not equal the total number of cases; due to rounding, the sum of percentages may not equal 100%. The P value represents the analysis of the significance of differences within the data groups from the three centers and the overall dataset. A P value below 0.05 is considered statistically significant. *, P<0.05. Basic diseases[†], diabetes, hypertension, and coronary heart disease. Center 1: Affiliated Hospital of Hebei University; Center 2: Baoding First Central Hospital; Center 3: The Fourth Affiliated Hospital of Hebei Medical University. BM, brain metastasis; CEA, carcinoembryonic antigen; CY211, cytokeratin 19 fragment; KPS score, Karnofsky Performance Status; LC, lung cancer; NSE, neuron-specific enolase; NSCLC, non-small cell lung cancer; SCLC, small-cell lung cancer.

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Table S4 Lesion-level MRI radiological characteristics in Part II

Characteristic	Center 1 (n=3,928)			Center 2 (n=879)			Center 3 (n=725)			Overall (N=5,532)		
	AD	SCC	P value	AD	SCC	P value	AD	SCC	P value	AD	SCC	P value
Location of BMs			0.011*			0.247			0.755			0.006*
Supratentorial area	3,049 (82.0)	192 (91.4)	0.630	681 (83.2)	54 (90.0)	0.964	573 (81.2)	16 (84.2)	0.988	4,293 (81.9)	262 (90.7)	0.609
Cortical or subcortical	2,473 (66.5)	150 (71.4)	0.872	555 (67.8)	45 (75.0)	0.322	517 (73.2)	14 (73.7)	0.291	3,535 (67.4)	209 (72.3)	0.974
Frontal lobe	1,000 (26.9)	64 (30.5)		242 (29.)	17 (28.3)		213 (30.2)	7 (36.8)		1,455 (27.8)	88 (30.5)	
Parietal lobe	600 (16.1)	35 (16.7)		138 (16.9)	10 (16.7)		97 (13.7)	3 (15.8)		835 (15.9)	48 (16.6)	
Temporal lobe	381 (10.3)	16 (7.6)		92 (111.2)	10 (16.7)		88 (12.5)	3 (15.8)		561 (10.7)	29 (10.0)	
Occipital lobe	492 (13.2)	35 (16.7)		83 (10.1)	8 (13.3)		119 (16.9)	1 (5.3)		684 (13.1)	44 (15.2)	
Deep brain	576 (15.5)	42 (20.0)	0.005*	126 (15.4)	9 (15.0)	0.726	56 (7.9)	2 (10.5)	0.451	758 (14.5)	53 (18.3)	0.008*
Centrum semiovale	177 (4.8)	20 (9.5)		13 (1.6)	1 (1.7)		12 (1.7)	0		202 (3.9)	21 (7.3)	
Periventricular	201 (5.4)	16 (7.6)		78 (9.5)	6 (10.0)		21 (3.0)	1 (5.3)		300 (5.7)	23 (8.0)	
Intraventricular	9 (0.2)	0		3 (0.4)	0		0	0		12 (0.2)	0	
Callosum	32 (0.9)	0		7 (0.9)	1 (1.7)		5 (0.7)	0		44 (0.84)	1 (0.4)	
Thalamus	68 (1.8)	4 (1.9)		6 (0.7)	0		7 (1.0)	0		81 (1.5)	4 (1.4)	
Basal ganglia region	89 (2.4)	2 (1.0)		19 (2.3)	1 (1.7)		11 (1.6)	1 (5.3)		119 (2.3)	4 (1.4)	
Infratentorial area	669 (18.0)	18 (8.6)	0.116	138 (16.9)	6 (10.0)	0.171	133 (18.8)	3 (15.8)	0.524	940 (17.9)	27 (9.3)	0.231
Cerebellum	588 (15.8)	18 (8.6)		132 (16.1)	5 (8.3)		117 (16.6)	3 (15.8)		837 (16.0)	26 (9.0)	
Brainstem	81 (2.2)	0		6 (0.7)	1 (1.7)		16 (2.3)	0		103 (2.0)	1 (0.4)	

Categorical variables are described as n (%). For qualitative variables, the Pearson χ^2 test or Fisher exact test was used to determine whether there were statistically significant differences. Due to the presence of missing values, the sum of case numbers in each group may not equal the total number of cases; due to rounding, the sum of percentages may not equal 100%. The P value represents the analysis of the significance of differences within the data groups from the three centers and the overall dataset. A P value below 0.05 is considered statistically significant. *, P<0.05. Center 1: Affiliated Hospital of Hebei University; Center 2: Baoding First Central Hospital; Center 3: The Fourth Affiliated Hospital of Hebei Medical University. AD, adenocarcinoma; BM, brain metastasis; MRI, magnetic resonance imaging; SCC, squamous cell cancer.

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Table S5 Patient-level clinical characteristics of patients with BM in Part II

Characteristic	Center 1 (n=506)			Center 2 (n=183)			Center 3 (n=71)			Overall (N=760)		
	AD	SCC	P value	AD	SCC	P value	AD	SCC	P value	AD	SCC	P value
Number of patients	467	39		159	24		63	8		689	71	
Gender			<0.001*			0.054			0.013*			<0.001*
Male	124 (26.6)	29 (74.4)		86 (54.1)	18 (75.0)		34 (54.0)	8 (100.0)		244 (35.4)	55 (77.5)	
Female	343 (73.4)	10 (25.6)		73 (45.9)	6 (25.0)		29 (46.0)	0		445 (64.6)	16 (22.5)	
Tobacco use			<0.001*			<0.001*			0.186			<0.001*
Nonsmoker	279 (59.7)	7 (17.9)		101 (63.5)	6 (25.0)		39 (61.9)	3 (37.5)		419 (60.8)	16 (22.5)	
Smoker	188 (40.3)	32 (82.1)		58 (36.5)	18 (75.0)		24 (38.1)	5 (62.5)		270 (39.2)	55 (77.5)	
Basic disease[†]			0.361			0.137			0.375			0.549
No	251 (53.7)	18 (46.2)		94 (59.1)	18 (75.0)		37 (58.7)	6 (75.0)		382 (55.4)	42 (59.2)	
Yes	216 (46.3)	21 (53.8)		65 (40.9)	6 (25.0)		26 (41.3)	2 (25.0)		307 (44.6)	29 (40.8)	
KPS score			0.546			0.829			0.532			0.584
≤70	116 (24.8)	8 (20.5)		34 (43.6)	4 (43.6)		31 (49.2)	3 (37.5)		181 (29.8)	15 (26.3)	
>70	351 (75.2)	31 (79.5)		44 (56.4)	6 (60.0)		32 (50.8)	5 (62.5)		427 (70.2)	42 (73.3)	
Extracranial metastases			0.357			0.382			0.532			0.071
No	169 (36.2)	17 (43.6)		91 (57.2)	16 (66.7)		32 (50.8)	5 (62.5)		292 (42.4)	38 (53.5)	
Yes	298 (63.8)	22 (56.4)		68 (42.8)	8 (33.3)		31 (49.2)	3 (37.5)		397 (57.6)	33 (46.5)	
Location of LC			0.072			0.305			0.589			0.111
Left lung	203 (43.5)	18 (46.2)		42 (26.4)	4 (16.7)		30 (47.6)	3 (37.5)		275 (39.9)	25 (35.2)	
Right lung	263 (56.3)	20 (51.3)		117 (73.6)	20 (83.3)		33 (52.4)	5 (62.5)		413 (59.9)	45 (63.4)	
Others	1 (0.2)	1 (2.6)		0	0		0	0		1 (0.1)	1 (1.4)	
Lung surgery			0.995			0.255			0.907			0.469
No	383 (82.0)	32 (82.1)		140 (88.1)	23 (95.8)		56 (88.9)	7 (87.5)		579 (84.0)	62 (87.3)	
Yes	84 (18.0)	7 (17.9)		19 (11.9)	1 (4.2)		7 (11.1)	1 (12.5)		110 (16.0)	9 (12.7)	
T staging of TNM			0.015*			0.858			0.192			0.007*
T1+T2	184 (59.5)	10 (35.7)		17 (20.5)	2 (18.2)		19 (59.4)	1 (25.0)		220 (51.9)	13 (30.2)	
T3+T4	125 (40.5)	18 (64.3)		66 (79.5)	9 (81.8)		13 (40.6)	4 (75.0)		204 (48.1)	30 (69.8)	
N staging of TNM			0.867			0.592			0.029*			0.132
N0+N1	84 (27.1)	8 (28.6)		91 (81.3)	16 (76.2)		7 (22.6)	3 (75.0)		182 (40.2)	27 (50.9)	
N2+N3	226 (72.9)	20 (71.4)		21 (18.8)	5 (23.8)		24 (77.4)	1 (25.0)		271 (59.8)	26 (49.1)	
M staging of TNM			0.048*			0.583			0.767			0.024*
M1b	74 (15.8)	12 (30.8)		39 (24.5)	8 (33.3)		32 (50.8)	5 (62.5)		145 (21.0)	25 (35.2)	
M1c1	95 (20.3)	5 (12.8)		52 (32.7)	8 (33.3)		7 (11.1)	1 (12.5)		154 (22.4)	14 (19.7)	
M1c2	298 (63.8)	22 (56.4)		68 (42.8)	8 (33.3)		24 (38.1)	2 (25.0)		390 (56.6)	32 (45.1)	
Clinical staging			0.017*			0.382			0.532			0.069
IVA	74 (15.8)	12 (30.8)		68 (42.8)	8 (33.3)		32 (50.8)	5 (62.5)		174 (25.3)	25 (35.2)	
IVB	393 (84.2)	27 (69.2)		91 (57.2)	16 (66.7)		31 (49.2)	3 (37.5)		515 (74.7)	46 (64.8)	
Ki-67			<0.001*			<0.001*			<0.001*			<0.001*
<25%	41 (35.7)	0		27 (27.0)	2 (11.8)		6 (20.7)	1 (33.3)		74 (30.3)	3 (7.7)	
25–50%	35 (30.4)	3 (15.8)		30 (30.0)	1 (5.9)		14 (48.3)	0		79 (32.4)	4 (10.3)	
>50%	39 (33.9)	16 (84.2)		43 (43.0)	14 (82.4)		9 (31.0)	2 (66.7)		91 (37.3)	32 (82.1)	
PD-L1			0.113			0.227			0.406			0.767
0%	36 (42.4)	1 (16.7)		8 (29.6)	2 (66.7)		9 (40.9)	1 (75.0)		53 (39.6)	4 (30.8)	
1–49%	35 (41.2)	2 (33.3)		5 (18.5)	1 (33.3)		9 (40.9)	3 (75.0)		49 (36.3)	6 (46.2)	
≥50%	14 (16.5)	3 (50.0)		14 (51.9)	0		4 (18.2)	0		32 (23.9)	3 (23.1)	
Gene mutation			0.564			0.210			0.023*			0.675
EGFR	183 (65.1)	21 (72.4)		8 (72.7)	2 (40.0)		37 (71.2)	0		228 (66.3)	23 (62.2)	
ALK	12 (4.3)	2 (6.9)		0	0		3 (5.8)	0		15 (4.4)	2 (5.4)	
KRAS	13 (4.6)	0		0	0		1 (1.9)	0		14 (4.1)	0	
ERBB/ROS1/TP53/MET/BRAF	13 (4.6)	2 (6.9)		0	0		2 (3.8)	0		15 (4.4)	2 (5.4)	
Negative	60 (21.4)	4 (13.8)		3 (27.3)	3 (60.0)		9 (17.3)	3 (100.0)		72 (20.9)	10 (27.0)	
EGFR			0.031*			0.223			0.011*			0.001*
Wild type	124 (33.8)	4 (80.0)		29 (33.3)	3 (60.0)		15 (28.8)	3 (100.0)		168 (33.2)	10 (76.9)	
Mutant type	243 (66.2)	1 (20.0)		58 (66.7)	2 (40.0)		37 (71.2)	0		338 (66.8)	3 (23.1)	
EGFR subtypes			0.623			0.679						0.404
19 exon	89 (37.7)	0		15 (30.0)	0		10 (27.0)	0		114 (35.3)	0	
21 exon	121 (51.3)	1 (100.0)		28 (56.0)	1 (100.0)		20 (54.1)	0		169 (52.3)	2 (100.0)	
18/20 exon	26 (11.0)	0		7 (14.0)	0		7 (18.9)	0		40 (12.4)	0	
Age (years)	61.9±9.8	65.0±7.6	0.053	63.3±9.4	66.0±8.4	0.222	59.4±8.3	58.9±7.7	0.500	62.0±9.6	64.7±8.1	0.040*
CEA (ng/mL)	14.50 (2.42, 14.58)	4.95 (2.42, 14.58)	<0.001	15.02 (4.23, 70.61)	5.12 (2.22, 16.51)	0.026*	13.47 (3.97, 77.74)	3.19 (2.41, 5.04)	0.021*	14.50 (4.32, 79.77)	4.90 (2.40, 14.58)	<0.001*
NSE (ng/mL)	17.50 (13.30, 27.40)	17.00 (13.7, 34.50)	0.470	23.01 (17.70, 32.50)	20.68 (18.43, 40.92)	0.827	16.20 (14.34, 23.76)	15.73 (13.23, 20.14)	0.598	18.77 (14.33, 28.92)	20.00 (14.49, 33.87)	0.316
CY211 (ng/mL)	5.60 (2.80, 12.90)	7.80 (4.13, 19.70)	0.067	5.39 (2.88, 10.50)	13.18 (3.49, 21.37)	0.011*	4.48 (2.77, 11.84)	4.14 (2.49, 24.39)	0.849	5.42 (2.80, 12.00)	7.80 (3.43, 19.70)	0.007*
Meningeal metastasis			0.952			0.697			0.371			0.995
No	442 (94.6)	37 (94.9)		158 (99.4)	24 (100.0)		60 (95.2)	7 (87.5)		660 (95.8)	68 (95.8)	
Yes	25 (5.4)	2 (5.1)		1 (0.6)	0		3 (4.8)	1 (12.5)		29 (4.2)	3 (4.2)	
Cranial bone metastasis			0.187			0.764			0.662			0.424
No	447 (95.7)	39 (100.0)		150 (94.3)	23 (95.8)		58 (92.1)	7 (87.5)		655 (95.1)	69 (97, 2)	
Yes	20 (4.3)	0		9 (5.7)	1 (4.2)		5 (7.9)	1 (12.5)		34 (4.9)	2 (2.8)	

Categorical variables are described as n (%). Continuous variables are presented as the median (Q1, Q3) or as the mean (standard deviation), denoted as mean ± SD. For continuous variables, the Student *t* test or Mann-Whitney U test was used to assess statistical significance; for qualitative variables, the Pearson χ^2 test or Fisher exact test was employed to determine if there were statistically significant differences. Due to the presence of missing values, the sum of case numbers in each group may not equal the total number of cases; due to rounding, the sum of percentages may not equal 100%. The P value represents the analysis of the significance of differences within the data groups from the three centers and the overall dataset. A P value below 0.05 is considered statistically significant. *, P<0.05. Basic diseases[†], diabetes, hypertension, and coronary heart disease. Center 1: Affiliated Hospital of Hebei University; Center 2: Baoding First Central Hospital; Center 3: The Fourth Affiliated Hospital of Hebei Medical University. AD, adenocarcinoma; ALK, anaplastic lymphoma kinase; BRAF, b-raf proto-oncogene; BM, brain metastasis; CEA, carcinoembryonic antigen; CY211, cytokeratin 19 fragment; EGFR, epidermal growth factor receptor; ERBB, erythroblastic leukemia viral oncogene homolog B; KPS score, Karnofsky performance status; KRAS, Kirsten rat sarcoma viral oncogene; LC, lung cancer; MET, MET proto-oncogene; NSE, neuron-specific enolase; PD-L1, programmed death-ligand 1; ROS1, ROS proto-oncogene 1; SCC, squamous cell cancer; TP53, tumor protein P53.

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Table S6 Lesion-level MRI radiological characteristics in Part III

Characteristic	Center 1 (n=3,029)			Center 2 (n=453)			Center 3 (n=655)			Overall (N=4,137)		
	Wild type	Mutant type	P value	Wild type	Mutant type	P value	Wild type	Mutant type	P value	Wild type	Mutant type	P value
Location of BMs, n (%)			0.165			0.030*			0.668			0.036*
Supratentorial area	780 (80.7)	1,697 (82.3)	0.576	149 (79.7)	227 (85.3)	0.299	90 (87.4)	444 (80.4)	0.212	1,019 (81.1)	2,368 (82.2)	0.095
Cortical or subcortical	620 (64.1)	1,381 (67.0)	0.695	105 (56.2)	177 (66.5)	0.518	75 (72.8)	406 (73.6)	0.060	800 (63.6)	1,964 (68.2)	0.765
Frontal lobe	242 (25.0)	555 (26.9)		47 (25.1)	78 (29.3)		25 (24.3)	173 (31.3)		314 (25.0)	806 (28.0)	
Parietal lobe	171 (17.7)	327 (15.9)		19 (10.2)	47 (17.7)		11 (10.7)	77 (14.0)		201 (16.0)	451 (15.7)	
Temporal lobe	92 (9.5)	216 (10.5)		23 (12.3)	33 (12.4)		18 (17.5)	68 (12.3)		133 (10.6)	317 (11.0)	
Occipital lobe	115 (11.9)	283 (13.7)		16 (8.6)	19 (7.1)		21 (20.4)	88 (15.9)		152 (12.1)	390 (13.5)	
Deep brain	160 (16.6)	316 (15.3)	0.462	44 (23.5)	50 (18.8)	0.452	15 (14.6)	38 (6.9)	0.057	219 (17.4)	404 (14.0)	0.976
Centrum semiovale	48 (5.0)	110 (5.3)		1 (0.5)	7 (2.6)		3 (2.9)	8 (1.5%)		52 (4.1)	125 (4.3)	
Periventricular	57 (5.9)	101 (4.9)		37 (19.8)	28 (10.5)		9 (8.7)	10 (1.8)		103 (8.2)	139 (4.8)	
Intraventricular	4 (0.4)	1 (0.1)		2 (1.1)	0		0	0		6 (0.5)	2 (0.1)	
Callosum	9 (0.9)	16 (0.8)		1 (0.5)	3 (1.1)		2 (1.9)	3 (0.5)		12 (1.0)	21 (0.7)	
Thalamus	15 (1.6)	43 (2.1)		1 (0.5)	4 (1.5)		1 (1.0)	6 (1.1)		17 (1.4)	53 (1.8)	
Basal ganglia region	27 (2.8)	45 (2.2)		2 (1.1)	8 (3.0)		0	11 (2.0)		29 (2.3)	64 (2.2)	
Infratentorial area	187 (19.3)	365 (17.7)	0.704	38 (20.3)	39 (14.7)	0.324	13 (12.6)	108 (19.6)	0.535	238 (18.9)	512 (17.8)	0.265
Cerebellum	167 (17.3)	322 (15.6)		38 (20.3)	38 (14.3)		12 (11.7)	93 (16.9)		217 (17.3)	453 (15.7)	
Brainstem	20 (2.1)	43 (2.1)		0	1 (0.4)		1 (1.0)	15 (2.7)		21 (1.7)	59 (2.1)	

Categorical variables are described as n (%). For qualitative variables, the Pearson χ^2 test or Fisher exact test was used to determine whether there were statistically significant differences. Due to the presence of missing values, the sum of case numbers in each group may not equal the total number of cases; due to rounding, the sum of percentages may not equal 100%. The P value represents the analysis of the significance of differences within the data groups from the three centers and the overall dataset. A P value below 0.05 is considered statistically significant. *, P<0.05. Center 1: Affiliated Hospital of Hebei University; Center 2: Baoding First Central Hospital; Center 3: The Fourth Affiliated Hospital of Hebei Medical University. BM, brain metastasis; MRI, magnetic resonance imaging.

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Table S7 Patient-level clinical characteristics of patients with BM in Part III

Characteristic	Center 1 (n=378)			Center 2 (n=92)			Center 3 (n=55)			Overall (N=532)		
	Wild type	Mutant types	P value	Wild type	Mutant types	P value	Wild type	Mutant types	P value	Wild type	Mutant types	P value
Number of patients	131	247		32	60		18	37		188	344	
Gender			<0.001*			<0.001*			0.005*			<0.001*
Female	54 (41.2)	53 (21.5)		25 (78.1)	20 (33.3)		14 (77.8)	14 (37.8)		93 (51.4)	87 (25.3)	
Male	77 (58.8)	194 (78.5)		7 (21.9)	40 (66.7)		4 (22.2)	23 (62.2)		88 (48.6)	257 (74.7)	
Tobacco use			<0.001*			<0.001*			0.008*			<0.001*
Nonsmoker	60 (45.8)	172 (69.6)		11 (34.4)	50 (83.3)		7 (38.9)	28 (75.7)		78 (43.1)	250 (72.7)	
Smoker	71 (54.2)	75 (30.4)		21 (65.6)	10 (16.7)		11 (61.1)	9 (24.3)		103 (56.9)	94 (27.3)	
Basic disease[†]			0.176			0.428			0.759			0.359
No	79 (60.3)	131 (53.0)		17 (53.1)	37 (61.7)		11 (61.1)	21 (56.8)		107 (59.1)	189 (54.9)	
Yes	52 (39.7)	116 (47.0)		15 (46.9)	23 (38.3)		7 (38.9)	16 (43.2)		74 (40.9)	155 (45.1)	
KPS score			0.977			0.737			0.294			0.620
≤70	29 (22.1)	55 (22.3)		8 (40.0)	13 (44.8)		8 (44.4)	22 (59.5)		45 (26.6)	90 (28.8)	
>70	102 (77.9)	192 (77.7)		12 (60.0)	16 (55.2)		10 (55.6)	15 (40.5)		124 (73.4)	223 (71.2)	
Extracranial metastases												
No	47 (35.9)	89 (36.0)	0.976	18 (56.3)	31 (51.7)	0.675	10 (55.6)	15 (40.5)	0.294	75 (41.4)	135 (39.2)	0.626
Yes	84 (64.1)	158 (64.0)		14 (43.8)	29 (48.3)		8 (44.4)	22 (59.5)		106 (58.6)	209 (60.8)	
Location of LC			0.073			0.858			0.925			0.107
Left lung	64 (48.9)	97 (39.3)		8 (25.0)	14 (23.3)		9 (50.0)	18 (48.6)		81 (44.8)	129 (37.5)	
Right lung	67 (51.1)	150 (60.7)		24 (75.0)	46 (76.7)		9 (50.0)	19 (51.4)		100 (55.2)	215 (62.5)	
Lung surgery			0.202			0.158			0.716			0.119
No	111 (84.7)	196 (79.4)		30 (93.8)	50 (83.3)		16 (88.9)	34 (91.9)		157 (86.7)	280 (81.4)	
Yes	20 (15.3)	51 (20.6)		2 (6.3)	10 (16.7)		2 (11.1)	3 (8.1)		24 (13.3)	64 (18.6)	
T staging of TNM			0.040*			0.848			0.469			0.061
T1+T2	48 (52.2)	117 (65.0)		5 (22.7)	8 (25.0)		6 (66.7)	11 (52.4)		59 (48.0)	136 (58.4)	
T3+T4	44 (47.8)	63 (35.0)		17 (77.3)	24 (75.0)		3 (33.3)	10 (47.6)		64 (52.0)	97 (41.6)	
N staging of TNM			0.609			0.043			0.260			0.716
N0+N1	25 (26.9)	54 (29.8)		18 (94.7)	31 (72.1)		3 (33.3)	3 (15.0)		46 (38.0)	88 (36.1)	
N2+N3	68 (73.1)	127 (70.2)		1 (5.3)	12 (27.9)		6 (66.7)	17 (85.0)		75 (62.0)	156 (63.9)	
M staging of TNM			0.685			0.687			0.431			0.591
M1b	18 (13.7)	41 (16.6)		4 (12.5)	10 (16.7)		10 (55.6)	15 (40.5)		32 (17.7)	66 (19.2)	
M1c1	29 (22.1)	48 (19.4)		14 (43.8)	21 (35.0)		3 (16.7)	5 (13.5)		46 (25.4)	74 (21.5)	
M1c2	84 (64.1)	158 (64.0)		14 (43.8)	29 (48.3)		5 (27.8)	17 (45.9)		103 (56.9)	204 (59.3)	
Clinical staging			0.466			0.675			0.294			0.702
IVA	18 (13.7)	41 (16.6)		14 (43.8)	29 (48.3)		10 (55.6)	15 (40.5)		42 (23.2)	85 (24.7)	
IVB	113 (6.3)	206 (83.4)		18 (56.3)	31 (51.7)		8 (44.4)	22 (59.5)		139 (76.8)	259 (75.3)	
Ki-67			0.934			0.331			0.404			0.939
<25%	12 (30.0)	19 (32.8)		7 (28.0)	8 (27.6)		2 (25.0)	3 (16.7)		21 (28.8)	30 (28.6)	
25–50%	13 (32.5)	17 (29.3)		6 (48.0)	12 (41.4)		5 (62.5)	8 (44.4)		24 (32.9)	37 (35.2)	
>50%	15 (37.5)	22 (37.9)		12 (48.0)	9 (31.0)		1 (12.5)	7 (38.9)		28 (38.4)	38 (36.2)	
PD-L1			0.226			0.668			0.349			0.450
0%	21 (53.8)	18 (36.0)		6 (33.3)	4 (40.0)		2 (22.2)	6 (35.7)		29 (43.9)	28 (37.8)	
1–49%	12 (30.8)	23 (46.0)		2 (11.1)	2 (20.0)		6 (66.7)	5 (35.7)		20 (30.3)	30 (40.5)	
≥50%	6 (15.4)	9 (18.0)		10 (55.6)	4 (40.0)		1 (11.1)	3 (21.4)		17 (25.8)	16 (21.6)	
Pathological subtypes			0.031*			0.223			0.011*			0.001*
AD	124 (96.9)	243 (99.6)		29 (90.6)	58 (96.7)		15 (83.3)	37 (100.0)		168 (94.4)	338 (99.1)	
SCC	4 (3.1)	1 (0.4)		3 (9.4)	2 (3.3)		3 (16.7)	0		10 (5.6)	3 (0.9)	
Age (years)	61.4±10.5	61.8±9.6	0.823	64.4±7.7	61.4±97	0.102	59.6±7.1	58.5±9.2	0.843	61.8±9.8	61.4±9.6	0.589
CEA (ng/mL)	8.97 (3.23, 56.30)	16.30 (5.34, 127.40)	0.018*	5.60 (2.39, 33.74)	17.12 (3.74, 76.19)	0.049	11.46 (3.89, 59.82)	14.42 (4.48, 81.26)	0.484	8.51 (3.24, 53.02)	16.51 (5.17, 93.51)	0.002*
NSE (ng/mL)	17.00 (12.74, 30.40)	33.91 (13.40, 28.00)	0.708	24.39 (17.24, 38.42)	21.25 (16.89, 26.81)	0.199	17.17 (13.91, 28.42)	16.57 (14.44, 27.59)	0.290	18.49 (13.70, 30.55)	18.75 (14.44, 27.61)	0.977
CY211 (ng/mL)	6.31 (3.25, 13.18)	5.28 (2.53, 13.18)	0.123	5.31 (3.03, 11.91)	3.89 (1.96, 9.66)	0.290	4.69 (2.40, 15.01)	4.43 (3.05, 10.66)	0.886	6.09 (3.11, 12.76)	4.81 (2.54, 12.05)	0.086
Meningeal metastases			0.023*			1.000			0.445			0.078
No	129 (98.5)	230 (93.1)		32 (100.0)	60 (100.0)		16 (88.9)	35 (94.6)		177 (97.8)	325 (94.5)	
Yes	2 (1.5)	17 (6.9)		0	0		2 (11.1)	2 (5.4)		4 (2.2)	19 (5.5)	
Cranial bone metastases			0.913			0.957			0.339			0.750
No	126 (96.2)	237 (96.0)		31 (96.9)	58 (96.7)		15 (83.3)	34 (89.1)		172 (95.0)	329 (95.6)	
Yes	5 (3.8)	10 (4.0)		1 (3.1)	2 (3.3)		3 (16.7)	3 (8.1)		9 (5.0)	15 (4.4)	

Categorical variables are described as n (%). Continuous variables are presented as the median (Q1, Q3) or as the mean (standard deviation), denoted as mean ± SD. For continuous variables, the Student *t* test or Mann-Whitney U test was used to assess statistical significance; for qualitative variables, the Pearson χ^2 test or Fisher exact test was employed to determine if there were statistically significant differences. Due to the presence of missing values, the sum of case numbers in each group may not equal the total number of cases; due to rounding, the sum of percentages may not equal 100%. The P value represents the analysis of the significance of differences within the data groups from the three centers and the overall dataset. A P value below 0.05 is considered statistically significant. *, P<0.05. Basic diseases[†], diabetes, hypertension, and coronary heart disease. Center 1: Affiliated Hospital of Hebei University; Center 2: Baoding First Central Hospital; Center 3: The Fourth Affiliated Hospital of Hebei Medical University. AD, adenocarcinoma; BM, brain metastasis; CEA, carcinoembryonic antigen; CY211, cytokeratin 19 fragment; EGFR, epidermal growth factor receptor; KPS, Karnofsky Performance Status; LC, lung cancer; NSE, neuron-specific enolase; PD-L1, programmed death-ligand 1; SCC, squamous cell cancer; TNM, tumor-node-metastasis.

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