Supplementary

A						В						С					
Variable		N	Hazard ratio		р	Variable		NH	Hazard ratio		р	Variable		N	Hazard ratio		р
NSE		1169		1 00 (1 00 1 00)	0.033	CYERA21-1		1169		1 00 (1 00 1 01)	<0.001	CEA		1169		1 00 (1 00 1 00)	0.089
Age	<50	323	Ť.	Reference	0.000	Age	<50	323	ī	Reference		Age	<50	323	ī	Reference	0.000
1.90	>60	427		0.88 (0.61, 1.27)	0.501		>60	427	-	0.89 (0.62, 1.29)	0.553	, ige	>60	427	-	0.88 (0.61, 1.26)	0.481
	50-60	419	-8-	0.90 (0.66, 1.23)	0.509		50-60	419		0.92 (0.67, 1.25)	0.582		50-60	419	-8-	0.90 (0.66, 1.23)	0.498
Gender	Male	702		Reference		Gender	Male	702		Reference		Gender	Male	702		Reference	
	Female	467	4	0.84 (0.68, 1.05)	0.122		Female	467	-	0.85 (0.69, 1.06)	0.144		Female	467	-	0.85 (0.68, 1.05)	0.125
Smoking	No	591		Reference		Smoking	No	591		Reference		Smoking	No	591		Reference	
	Yes	180	L∰-	1.27 (0.99, 1.62)	0.058		Yes	180	ب ھ-	1.26 (0.99, 1.61)	0.061		Yes	180	- ₩-	1.29 (1.01, 1.64)	0.043
	Quit	398	.	1.19 (0.96, 1.47)	0.113		Quit	398	1	1.19 (0.96, 1.48)	0.103		Quit	398	1 <u>8</u> -	1.22 (0.98, 1.51)	0.069
KPS	<70	78		Reference		KPS	<70	78		Reference		KPS	<70	78		Reference	
	>90	33		0.76 (0.45, 1.31)	0.326		>90	33		0.77 (0.45, 1.32)	0.339		>90	33		0.73 (0.43, 1.25)	0.253
	70-90	1058	-	0.94 (0.70, 1.25)	0.672		70-90	1058	-	0.94 (0.70, 1.25)	0.670		70-90	1058	-	0.94 (0.70, 1.25)	0.664
EM	No	212	, 🖷	Reference		EM	No	212	÷.	Reference		EM	No	212	, i	Reference	
	Yes	957		1.27 (0.87, 1.84)	0.212		Yes	957	- -	1.27 (0.87, 1.84)	0.214		Yes	957	- - -	1.27 (0.87, 1.84)	0.214
MT_numbe	r >3	560		Reference		MT_numbe	r>3	560		Reference		MT_numbe	r>3	560		Reference	
	1	441	-#-	0.84 (0.59, 1.19)	0.328		1	441	-#-	0.85 (0.60, 1.21)	0.363		1	441	-#-	0.85 (0.60, 1.20)	0.358
	2-3	168	-	0.88 (0.70, 1.11)	0.279		2-3	168	-	0.90 (0.72, 1.13)	0.359		2-3	168	-	0.90 (0.71, 1.13)	0.345
BMI		1169		0.98 (0.96, 1.00)	0.089	BMI		1169		0.98 (0.96, 1.00)	0.097	BMI		1169		0.98 (0.96, 1.00)	0.058
EGFR	Neg	238		Reference		EGFR	Neg	238	-	Reference		EGFR	Neg	238		Reference	
	Pos	265	-	0.66 (0.53, 0.82)	<0.001		Pos	265	- -	0.66 (0.53, 0.83)	<0.001		Pos	265	.	0.66 (0.53, 0.82)) <0.001
	Unknown	666	-	0.94 (0.75, 1.17)	0.570		Unknown	666	-	0.97 (0.78, 1.22)	0.809		Unknown	666	-	0.96 (0.77, 1.21)	0.739
ALK	Neg	369		Reference		ALK	Neg	369		Reference		ALK	Neg	369		Reference	
	Pos	60		0.58 (0.41, 0.83)	0.003		Pos	60		0.59 (0.42, 0.85)	0.004		Pos	60	-8-1	0.60 (0.42, 0.86)	0.006
	Unknown	740		0.97 (0.75, 1.25)	0.806		Unknown	740	+	0.97 (0.76, 1.25)	0.836		Unknown	740	+	0.98 (0.77, 1.26)	, 0.893
ROS	Neg	311		Reference		ROS	Neg	311		Reference		ROS	Neg	311		Reference	
	Pos	14		0.61 (0.30, 1.25)	0.181		Pos	14		0.62 (0.31, 1.27)	0.194		Pos	14		0.61 (0.30, 1.24)	0.172
	Unknown	844	-	1.33 (1.04, 1.69)	0.021		Unknown	844		1.32 (1.04, 1.68)	0.024		Unknown	844		1.30 (1.03, 1.66)	, 0.030
GPA score	0-1	413		Reference		GPA score	0-1	413		Reference		GPA score	0-1	413		Reference	
	1.5-2	518		0.94 (0.67, 1.33)	0.734		1.5-2	518		0.92 (0.66, 1.30)	0.647		1.5-2	518		0.93 (0.66, 1.31)	0.690
	2.5-3.0	217		0.82 (0.43, 1.58)	0.554		2.5-3.0	217		0.82 (0.43, 1.59)	0.563		2.5-3.0	217		0.81 (0.42, 1.56)	0.534
	3.5-4.0	21		0.69 (0.23, 2.07)	0.512		3.5-4.0	21		0.69 (0.23, 2.07)	0.512		3.5-4.0	21		0.68 (0.23, 2.02)	0.485

Figure S1 Multivariate Cox's forest plots of overall survival in lung cancer patients with brain metastases based on baseline levels of different serum tumor markers as continuous variables.



Figure S2 Kaplan-Meier curves and multivariate Cox's forest plots of overall survival based on baseline levels of CEA, stratified by nonsmall cell lung cancer (NSCLC) and small cell lung cancer (SCLC) patients with brain metastases, respectively.



Figure S3 Kaplan-Meier curves and multivariate Cox's forest plots of overall survival based on baseline levels of NSE, stratified by non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) patients with brain metastases, respectively.



Figure S4 Kaplan-Meier curves and multivariate Cox's forest plots of overall survival based on baseline levels of serum levels of CYFRA21-1, stratified by non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) patients with brain metastases, respectively.

Variable		Ν	Hazard ratio		р
Age	<50	30		Reference	
	>60	50		1.14 (0.30, 4.31)	0.850
	50-60	53		0.84 (0.27, 2.63)	0.758
Gender	Male	101		Reference	
	Female	32	• •• •	1.58 (0.72, 3.47)	0.251
Smoking	No	43		Reference	
	Yes	29	+ -	1.59 (0.66, 3.81)	0.303
	Quit	61		1.73 (0.80, 3.72)	0.162
KPS	<70	10		Reference	
	>90	4		0.68 (0.07, 6.75)	0.744
	70-90	119	-	0.90 (0.25, 3.28)	0.873
EM	No	26		Reference	
	Yes	107	-	1.23 (0.33, 4.53)	0.761
BMI		133		1.02 (0.95, 1.09)	0.647
MT_number	>3	60		Reference	
	1	55		1.33 (0.40, 4.38)	0.641
	2-3	18	+ -	0.90 (0.33, 2.43)	0.833
CYFRA21-1_class	1	87		Reference	
	2	12		5.01 (1.84, 13.64)	0.002
	3	34	r a ti	2.32 (1.13, 4.78)	0.022
CEA_class	1	108		Reference	
	2	6	-	0.63 (0.20, 1.97)	0.425
	3	19	• • •	1.07 (0.51, 2.25)	0.849
NSE_class	1	1	—	Reference	
	2	118		21.95 (1.96, 245.64)	0.012
	3	14		10.22 (0.88, 118.94)	0.063
CYFRA21-1	High	80		Reference	
	Low	53	-	1.07 (0.59, 1.96)	0.822
CEA	High	65		Reference	
	Low	68		0.84 (0.49, 1.44)	0.518
NSE	High	70		Reference	
	Low	63		0.64 (0.37, 1.09)	0.102
Immunotherapy	No	122	_	Reference	
	Yes	11		0.88 (0.32, 2.42)	0.799
Radiotherapy	No	49		Reference	
	Yes	84		0.91 (0.55, 1.48)	0.691
Chemotherapy	No	8		Reference	
	Yes	125		0.12 (0.04, 0.35)	<0.001
Targeted therapy	No	86		Reference	
	Yes	47		0.98 (0.60, 1.62)	0.948
GPA_C	0-1	49		Reference	
	1.5-2	52		0.54 (0.16, 1.84)	0.323
	2.5-3.0	31		0.81 (0.08, 7.87)	0.857
	3.5-4.0	1		1.09 (0.02, 70.15)	0.966

Figure S5 Multivariate Cox's forest plots of overall survival in lung cancer patients with brain metastases lacking key driver genes based on dynamic changes of different serum tumor markers.