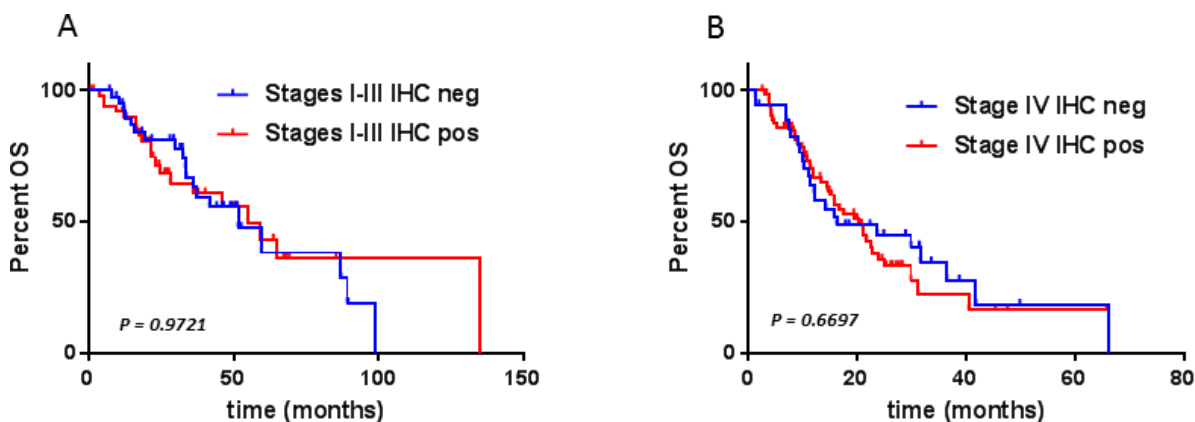


MET amplification assessed using optimized FISH reporting criteria predicts early distant metastasis in patients with non-small cell lung cancer

SUPPLEMENTARY MATERIALS



Supplementary Figure 1: Kaplan-Meier curves comparing overall survival (OS) by MET IHC status. (A) Comparison of OS in patients with (pos, positive) and without (neg, negative) MET overexpression in the stages I-III NSCLC group; **(B)** Comparison of OS in patients with (pos, positive) and without (neg, negative) MET overexpression in the stage IV NSCLC group.

Supplementary Table 1: *MET* copy number distribution according to optimized and historic criteria*

Optimized reporting criteria	No. of patients (%) (N = 384)		
	<i>MET</i> neg	<i>MET</i> cng	<i>MET</i> amp
	338 (88.0)	17 (4.4)	29 (7.6)
Historic reporting criteria			
<i>MET</i> -negative			
<i>MET</i> CN < 3	273 (71.1)	0	0
<i>MET</i> CN ≥ 3 to < 4	65 (16.9)	0	0
<i>MET</i> CN ≥ 4 to < 5	0	17 (4.4)	0
<i>MET</i> CN ≥ 5	0	0	8 (2.1)
<i>MET</i> -positive			
<i>MET</i> /CEP7 ratio ≥ 2.0	0	0	21 (5.5)

Abbreviations: *MET*, mesenchymal-epithelial transition factor; *MET* CN: *MET* copy number per cell, *MET*neg, *MET*-negative; *MET*cng, *MET* copy number gain; *MET*amp, *MET* amplification; CEP7, centromere probe of chromosome 7.

*Both reporting criterion included those with “the *MET*/CEP7 ratio was < 2.0 but the *MET*-CN was ≥ 20 copies/cell or *MET* signal clusters were seen in more than 10% of tumor cells”.

Supplementary Table 2: Comparison of overall survival by *MET* status in patients with stages I-III NSCLC

Five-Group <i>MET</i> Classification	No. of Patients	OS1 ^a (Months)	P1 ^b	P2 ^c	Optimized <i>MET</i> Categories	OS2 ^d (Months)	P3 ^e
					<i>MET</i> neg	51.6	Ref.
<i>MET</i> CN < 3 (Group1)	121	48.9	.034*	Ref.			
<i>MET</i> CN ≥ 3 to < 4 (Group2)	32	59.1	.005*	.321			
					<i>MET</i> cng	134.4	.106
<i>MET</i> CN ≥ 4 to < 5 (Group3)	10	134.4	.003*	.063			
					<i>MET</i> amp	28.1	.036*
<i>MET</i> CN ≥ 5 (Group4)	2	28.1	.782	.623			
<i>MET</i> /CEP7 ratio ≥ 2.0 (Group5)	5	23.6	Ref.	.034*			

Abbreviations: *MET*, mesenchymal-epithelial transition factor; *MET* CN: *MET* copy number per cell; OS, overall survival; *MET*amp, *MET* amplification; *MET*cng, *MET* copy number gain; *MET*neg, *MET*-negative; CEP7, centromere probe of chromosome 7.

^aOS1: OS according to the 5-group *MET* classification. ^bP1: *P* value for the 5-group classification with *MET*/CEP7 ratio ≥ 2.0 as the reference category.

^cP2: *P* value for the 5-group classification with *MET*CN < 3 as the reference category.

^dOS2: OS according to the optimized *MET* categories.

^eP3: *P* value in the optimized categories with *MET*neg as the reference category. * Indicates statistically significant result (*P* < .05).

Supplementary Table 3: Comparison of *MET* parameters by disease stage

<i>MET</i> Parameter	Overall	Stage I-III	Stage IV	<i>P</i> Value
<i>MET</i> FISH Quantity				
Mean <i>MET</i> -CN per cell (range)	3.13 (1.48-20.5)	2.83 (1.50-13.68)	3.36 (1.48-20.5)	.042*
Mean CEP7 per cell (range)	2.65 (1.37-9.6)	2.64 (1.65-7.48)	2.67 (1.37-9.60)	.743
Mean <i>MET</i> /CEP7 ratio(range)	1.15 (0.5-8.5)	1.06 (0.50-2.28)	1.21 (0.68-8.50)	.016*
<i>MET</i> FISH Categories				
<i>MET</i> neg, n (%)	338	153 (90.0)	185 (86.4)	.038*
<i>MET</i> cng, n (%)	17	10 (5.9)	7 (3.3)	
<i>MET</i> amp, n (%)	29	7 (4.1)	22 (10.3)	

Abbreviations: *MET*, mesenchymal-epithelial transition factor; *MET* CN: *MET* copy number per cell; CEP7, centromere probe of chromosome 7; FISH, fluorescence *in situ* hybridization; *MET*neg, *MET*-negative; *MET*cng, *MET* copy number gain; *MET*amp, *MET* amplification. * Indicates statistically significant result ($P < .05$, Fisher exact test or *t* test).

Supplementary Table 4: Overall survival and patient clinicopathological characteristics

Characteristic	No. of Patients	Median OS (months)	P Value
Age (years)			.184
≤ 64	199	34.8	
> 64	185	30.9	
Sex			.575
Male	184	29.9	
Female	200	36.0	
Race/ethnicity			.450
White	305	32.1	
Non-white ^a	72	31.6	
Histology			<.001*
Adenocarcinoma	338	34.8	
Others ^b	46	24.7	
Stage			<.001*
I-III	170	51.6	
IV	214	19.5	

^a Non-white included 25 black, 24 Hispanic, and 23 Asian patients. Seven patients with unknown race were excluded from the analysis.

^b Others included 40 patients with squamous cell carcinoma, 5 patients with unclassified non-small cell lung cancer, and 1 patient with adenosquamous carcinoma.

* Indicates statistically significant result ($P < .05$).

Supplementary Table 5: MET protein overexpression in patients with different stages and MET copy number groups

	Total, N (%)	Stages, N (%)		P Value	MET-CN Status, N (%)			P Value
	N = 384	I-III N = 170	IV N = 214		METneg N = 338	METcng N = 17	METamp N = 29	
MET-IHC				0.14				0.28
negative	78 (20.3)	41 (24.1)	37 (17.3)		20 (20.7)	3 (17.7)	5 (17.2)	
positive	124 (32.3)	51 (30.0)	73 (34.1)		102 (30.2)	5 (29.4)	17 (58.6)	
not available	182 (47.4)	78 (45.9)	104 (48.6)		166 (49.1)	9 (52.9)	7 (24.1)	

Abbreviations: MET, mesenchymal-epithelial transition factor; MET CN: MET copy number per cell, METneg, MET-negative; METcng, MET copy number gain; METamp, MET amplification; IHC, immunohistochemistry.