

Tumor MET Expression and Gene Amplification in Chinese Patients with Locally Advanced or Metastatic Gastric or Gastroesophageal Junction Cancer

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Abstract

MET and its sole ligand, hepatocyte growth factor (HGF), are promising targets in gastric and gastroesophageal junction cancer. We evaluated whether MET protein expression or *MET* gene amplification is prognostic for overall survival (OS) in Chinese patients with advanced gastric or gastroesophageal junction cancer. Archival formalin-fixed, paraffin-embedded tumor samples from patients with unresectable locally advanced or metastatic gastric or gastroesophageal junction cancer enrolled in clinical trials at Peking University Cancer Hospital from 2008 to 2010 were assessed for MET and phospho-MET (p-MET) expression by immunohistochemistry and *MET* amplification by FISH. MET-positive expression was defined as membrane protein staining in $\geq 25\%$ of tumor cells. *MET* amplification was defined as *MET*:centromere 7 ratio > 2.0 . We tested the association of MET status with clinical characteristics and OS, and also evaluated the association between

expression and amplification. One hundred sixty-eight patients were eligible. Of the evaluable samples, 53 of 137 (39%) were MET positive, eight of 134 (6%) were p-MET positive, and eight of 113 (7%) were *MET* amplified. Neither MET expression nor *MET* amplification were associated with clinical characteristics, except Lauren classification ($P = 0.04$); *MET* amplification was associated with diffuse type. No significant OS difference was observed between MET-positive and MET-negative populations, regardless of first-line chemotherapy received. In 95 evaluable patients, MET expression was significantly associated with *MET* amplification ($P < 0.001$); all *MET*-amplified tumor samples showed some MET expression. In 96 evaluable patients, p-MET positivity was significantly associated with *MET* amplification ($P < 0.001$). Further evaluation in larger and independent sample sets is warranted to confirm our findings. *Mol Cancer Ther*; 14(11); 2634–41. ©2015 AACR.

Introduction

More than 40% percent of the world's gastric cancer cases occur in China. Gastric cancer is the third most common cancer in China, with 405,000 estimated new cases in 2012 (1). Furthermore, gastric cancer causes more than 325,000 deaths annually in China (1). Despite recent advancements in therapy, median survival of patients with advanced gastric cancer remains poor at approximately 9 to 12 months (2–9).

Hepatocyte growth factor (HGF), also known as scatter factor, and its receptor MET appear to be promising therapeutic targets in

oncology (10). Activation of the HGF/MET signaling pathway promotes the proliferation, migration, and survival of tumor cells (10). It has also been shown to be associated with cancer pathogenesis, invasion, and metastasis (11).

Potential prognostic and predictive biomarkers in advanced gastric cancer have been identified. For example, overexpression of HER2 has been shown to be predictive of outcomes in patients with advanced gastric cancer treated with trastuzumab (2). Furthermore, *MET* gene amplification and increased MET protein expression have been associated with advanced disease and poor prognosis in metastatic gastric cancer (12–16).

Although others have explored the relationship between MET expression or *MET* amplification and prognosis in gastric cancer, most of these studies evaluated early-stage patients or mixed-stage populations (13–20), so the prognostic effect of MET in late-stage disease remains unclear. Cancer stage may be an important factor when studying the prognostic effect of MET, as MET is associated with tumor invasion (11). Moreover, prior studies primarily evaluated samples from resected tissue (13–20). Biopsy samples are more relevant in advanced disease, and limited data about MET status in biopsy samples were available in these studies.

In the current study, we obtained biopsy samples from patients with locally advanced or metastatic gastric or gastroesophageal junction cancer who were treated at a large cancer center in China, and we retrospectively tested the samples for MET expression, phospho-MET (p-MET) expression, and *MET* gene amplification.

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Our objective was to evaluate whether MET expression and *MET* amplification are prognostic for overall survival (OS).

Materials and Methods

Patients

Eligible patients had unresectable locally advanced or metastatic gastric or gastroesophageal junction cancer and were enrolled in multicenter phase II/III clinical trials between 2008 and 2010 at the Peking University Cancer Hospital in Beijing, China. Trials included the following, as identified by their ClinicalTrials.gov identifiers: NCT00548548, NCT01041404, NCT00887822, NCT00678535, NCT01015339, and NCT00842491. Biopsy tumor samples were obtained from all patients by endoscopy from the primary gastric cancer site, prior to chemotherapy. The number of metastatic sites was determined by the number of involved organs at trial enrollment. Tissues were fixed with formalin and paraffin-embedded in blocks, which were prepared at the time of biopsy. Patients with available baseline characteristics and clinical data were included in the analysis. All patients provided written informed consent for the trial participation, and the trials were approved by the Institutional Review Board of the Peking University Cancer Hospital. All patients were followed until December 31, 2013.

Analytical methods

MET protein expression, *MET* gene amplification, phospho-MET (p-MET) expression, and HER2 expression were retrospectively evaluated.

MET expression was determined by an automated MET immunohistochemistry (IHC) Investigational Use Only (IUO) assay using antibody clone MET4 (Dako), as previously described (21). Samples were defined as MET positive if $\geq 25\%$ of tumor cells had membrane protein staining at any intensity (21). *MET* amplification was analyzed by FISH using the Research Use Only (RUO) *MET*/CEN-7 IQFISH Probe Mix assay (Dako). Samples were defined as *MET* amplified in this analysis if the *MET*:centromere 7 ratio was >2.0 . Several cutoffs have been probed to define *MET* amplification using the Colorado scoring system as a guide (22). One cutoff that appears to define focal amplification is a *MET*:centromere 7 ratio >2.0 (21). This cutoff also mirrors the HER2 amplification cutoff, which is widely used in gastric cancer. Prior to assay implementation, technicians and pathologists were trained and certified as proficient by Dako.

Phospho-MET expression was analyzed by IHC using a research grade assay that utilized the monoclonal p-MET antibody (Tyr1234/1235; D26; Cell Signaling Technology, Inc.) Immunopositive cases were defined as those exhibiting membrane protein staining in $>10\%$ of tumor cells in the sample.

HER2 expression was analyzed by IHC using the PATHWAY anti-HER-2/neu (4B5) rabbit monoclonal primary antibody (Ventana Medical Systems, Inc.) HER2 positivity was defined as IHC 3+ staining alone or the combination of IHC 2+ staining and FISH positive. In cases of IHC 2+ staining, FISH was performed with PathVysion (Abbott Laboratories). Tumor specimens with a *HER2*:centromere 17 ratio >2.0 were considered *HER2* FISH-positive.

All samples were analyzed and evaluated in the Department of Pathology at Peking University Cancer Hospital. Pathologists were blinded to the clinical and molecular characteristics of the patients.

Statistical analysis

The Fisher exact test was used to evaluate the following: (i) association between MET expression and *MET* amplification, (ii) association of MET expression and *MET* amplification with clinical characteristics, and (iii) association between MET expression or *MET* amplification and p-MET expression. Survival curves for OS were plotted using the Kaplan–Meier method and were compared using the log-rank test. The HR for OS between MET-positive and MET-negative patients was evaluated using the Cox proportional hazards model. Statistical significance was defined as $P < 0.05$. For the 95% confidence interval (CI) of a proportion, a binomial exact CI was provided.

Results

Patient characteristics

Overall, 168 patients were eligible for the study. Of these, 155 patients had available tumor samples for testing: 137 patients had samples evaluable for MET IHC, 113 patients had samples evaluable for *MET* FISH, and 134 patients had samples evaluable for p-MET IHC. A patient flow diagram is shown in Fig. 1. Patient demographics, disease characteristics, and treatment are shown in Table 1. All patients with available tumor samples received first-line systemic chemotherapy for metastatic disease. Besides one patient receiving paclitaxel alone, all other patients received doublet or triplet chemotherapy. Among the 137 patients with evaluable MET IHC, 60% received first-line platinum-based therapy (fluoropyrimidine/platinum or fluoropyrimidine/platinum/taxane), and 53% received first-line taxane-based therapy (fluoropyrimidine/taxane, fluoropyrimidine/taxane/platinum, or taxane alone; Table 1).

Incidence of MET protein expression and *MET* gene amplification

Of the 137 patients evaluable for MET IHC, 53 patients (39%; 95% CI, 30%–47%) had MET-positive tumors. Forty-one patients (30%) had tumors with no MET membrane staining of any intensity and 43 patients (31%) had tumors with $>0\%$ and $<25\%$ of cells with MET membrane staining of any intensity. Of the 113 patients evaluable for *MET* FISH, 8 patients (7%; 95% CI, 3%–13%) had tumors with *MET* amplification.

Association between MET expression/*MET* amplification and clinical characteristics

Among the 137 patients with evaluable IHC samples, no significant association was observed between MET expression and clinical characteristics (Table 1). Among the 113 patients with evaluable FISH samples, *MET* amplification was not associated with sex, primary tumor site, distant metastasis (liver vs. lung), or number of metastases (Table 1). However, among the 111 patients for whom Lauren classification data were available, Lauren classification was associated with *MET* amplification ($P = 0.04$; Table 1); seven of 46 diffuse samples (15%) were *MET* amplified, whereas one of 49 intestinal samples (2%) were *MET* amplified.

Association between MET expression and *MET* amplification

Ninety-five patients had samples evaluable for both MET IHC and *MET* FISH, and of these, eight patients had *MET*-amplified tumors. MET expression was significantly associated with *MET* amplification ($P < 0.001$). All eight tumor samples with *MET* amplification had $\geq 90\%$ MET expression (Fig. 2).

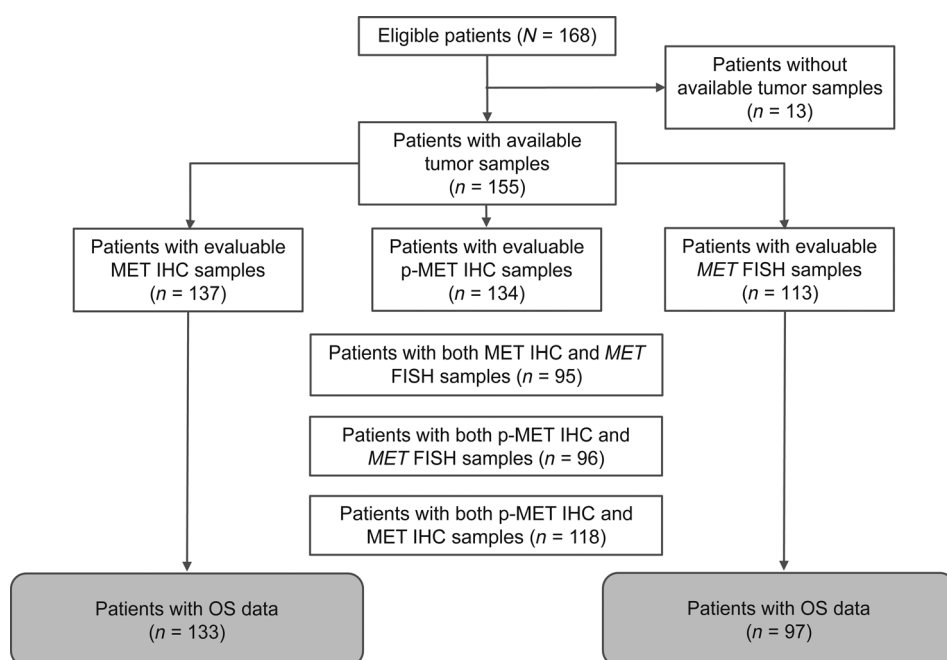


Figure 1. Patient flow diagram. Eligible patients had unresectable locally advanced or metastatic gastric or gastroesophageal junction cancer. Tumor samples were obtained by biopsy, prior to chemotherapy.

Survival analyses

Of the 141 patients with available survival data, the median follow-up time was 10.9 months. Of 15 censored patients with available survival data, the median follow-up time was 35.0

months. Follow-up time was measured from the start date of chemotherapy for advanced gastric cancer.

Of the 137 evaluable patients for MET IHC, 133 had available survival data. In this population, no statistically significant

Table 1. Patient demographics, disease characteristics, and treatment by IHC and FISH subgroups

	IHC analysis				FISH analysis			
	All evaluable patients ^a (n = 137)	MET-positive expression ^b (n = 53)	MET-negative expression ^b (n = 84)	P ^c	All evaluable patients ^a (n = 113)	MET-positive amplification ^b (n = 8)	MET-negative amplification ^b (n = 105)	P ^c
Median age, yr	58	58	58		58	62	58	
Sex, n (%)				0.14				0.68
Male	106 (77)	45 (42)	61 (58)		89 (79)	6 (7)	83 (93)	
Female	31 (23)	8 (26)	23 (74)		24 (21)	2 (8)	22 (92)	
Primary tumor site, n (%)				0.85				1.00
Stomach	91 (66)	36 (40)	55 (60)		80 (71)	6 (8)	74 (92)	
Gastroesophageal junction	46 (34)	17 (37)	29 (63)		33 (29)	2 (6)	31 (94)	
Lauren classification ^d , n (%)				0.45				0.04
Intestinal	57 (43)	20 (35)	37 (65)		49 (44)	1 (2)	48 (98)	
Diffuse	54 (40)	24 (44)	30 (56)		46 (41)	7 (15)	39 (85)	
Mixed	23 (17)	7 (30)	16 (70)		16 (14)	0 (0)	16 (100)	
Number of organs with metastasis, n (%)				1.00				0.72
1-2	92 (67)	36 (39)	56 (61)		76 (67)	5 (7)	71 (93)	
≥3	45 (33)	17 (38)	28 (62)		37 (33)	3 (8)	34 (92)	
Distant metastasis, n (%)								
Liver	61 (45)	26 (43)	35 (57)		55 (49)	5 (9)	50 (91)	
Lung	10 (7)	5 (50)	5 (50)		9 (8)	1 (11)	8 (89)	
Treatment, n (%)								
First-line platinum-based therapy ^e	82 (60)	35 (43)	47 (57)		—	—	—	
First-line taxane-based therapy ^{e,f}	73 (53)	23 (32)	50 (68)		—	—	—	
First-line platinum + taxane (triplet therapy)	18 (13)	5 (28)	13 (72)		—	—	—	
Monotherapy	1 (1)	1 (100)	0		—	—	—	
Chemotherapy/trastuzumab	6 (4)	3 (50)	3 (50)		—	—	—	

^aPercentages reflect each patient subgroup as the percentage of all evaluable patients (percentages calculated by column).

^bPercentages reflect each MET subgroup as the percentage of the subset of patients in each patient subgroup (percentages calculated by row).

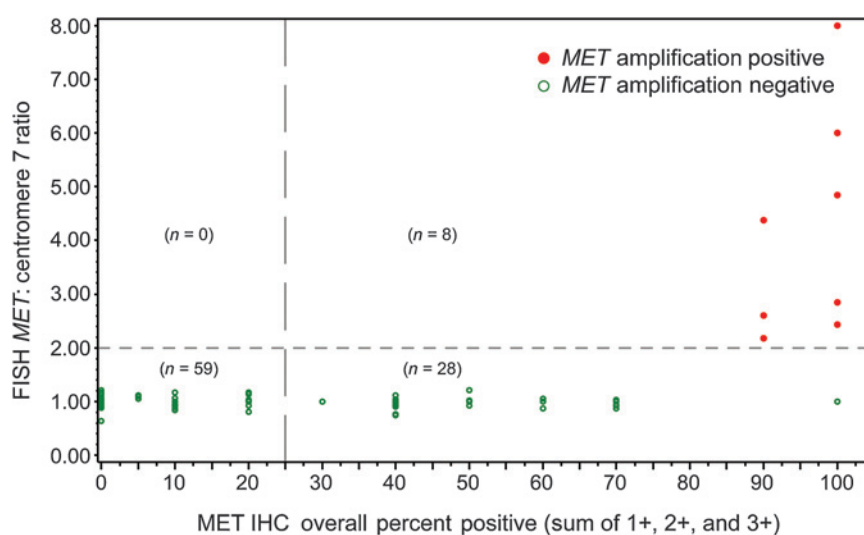
^cFisher exact test.

^dNumber of patients with Lauren classification available: IHC analysis - total, n = 134; MET-negative, n = 83; MET-positive, n = 51; FISH analysis - total, n = 111; MET amplification negative, n = 103; MET amplification positive, n = 8.

^eIncludes platinum- and taxane-based triplet (n = 18).

^fIncludes paclitaxel alone (n = 1).

Figure 2. Association between MET expression and MET amplification. Scatter plot shows the percentage of MET IHC overall positive versus FISH *MET*:centromere 7 ratio ($n = 95$). MET expression was significantly associated with MET amplification ($P < 0.001$).



difference in OS was observed between the MET-positive and MET-negative patients ($P = 0.80$; Fig. 3A). The HR (95% CI) was 1.049 (0.725–1.518), and the median OS times were 12.3 and 10.9 months in the MET-positive and MET-negative patients, respectively (Supplementary Table S1).

We also evaluated the prognostic value of MET expression according to treatment disposition. In patients receiving first-line platinum/fluoropyrimidine therapy ($n = 62$), there was a nonsignificant trend toward shorter OS in the MET-positive patients versus MET-negative patients ($P = 0.12$; Fig. 3B); the HR (95% CI) was 1.530 (0.892–2.625), and the median OS times were 10.6 and 11.9 months, respectively (Supplementary Table S1). In patients receiving first-line taxane-based therapy ($n = 71$), no statistically significant difference in OS was observed between the MET-positive patients and MET-negative patients ($P = 0.26$; Fig. 3C); the HR (95% CI) was 0.736 (0.431–1.256), and the median OS times were 12.6 and 10.8 months, respectively (Supplementary Table S1). In patients receiving first-line platinum-based therapy ($n = 80$), no statistically significant difference in OS and no apparent trends were observed between the MET-positive and MET-negative patients ($P = 0.37$; Fig. 3D); the HR (95% CI) was 1.243 (0.774–1.996), and the median OS times were 11.3 and 11.8 months, respectively (Supplementary Table S1).

Association between MET expression/MET amplification and p-MET expression

Of the 134 patients evaluable for p-MET IHC, eight (6%; 95% CI, 3%–11%) had p-MET-positive tumors. Representative p-MET IHC images are shown in Fig. 4A.

Ninety-six patients were evaluable for both p-MET IHC and MET FISH, and of these patients, seven had p-MET-positive tumors. Of the seven patients with p-MET-positive tumors, all had MET amplification; only one patient with a MET-amplified tumor was not p-MET-positive (Table 2, Fig. 4B). There was a significant association between p-MET expression and MET amplification ($P < 0.001$).

Of 118 patients evaluable for both p-MET IHC and MET IHC, 8 had p-MET-positive tumors (Fig. 4C). Of the 8 patients with p-MET-positive tumors, all had MET expression. There was a

significant association between p-MET expression and MET expression ($P < 0.001$).

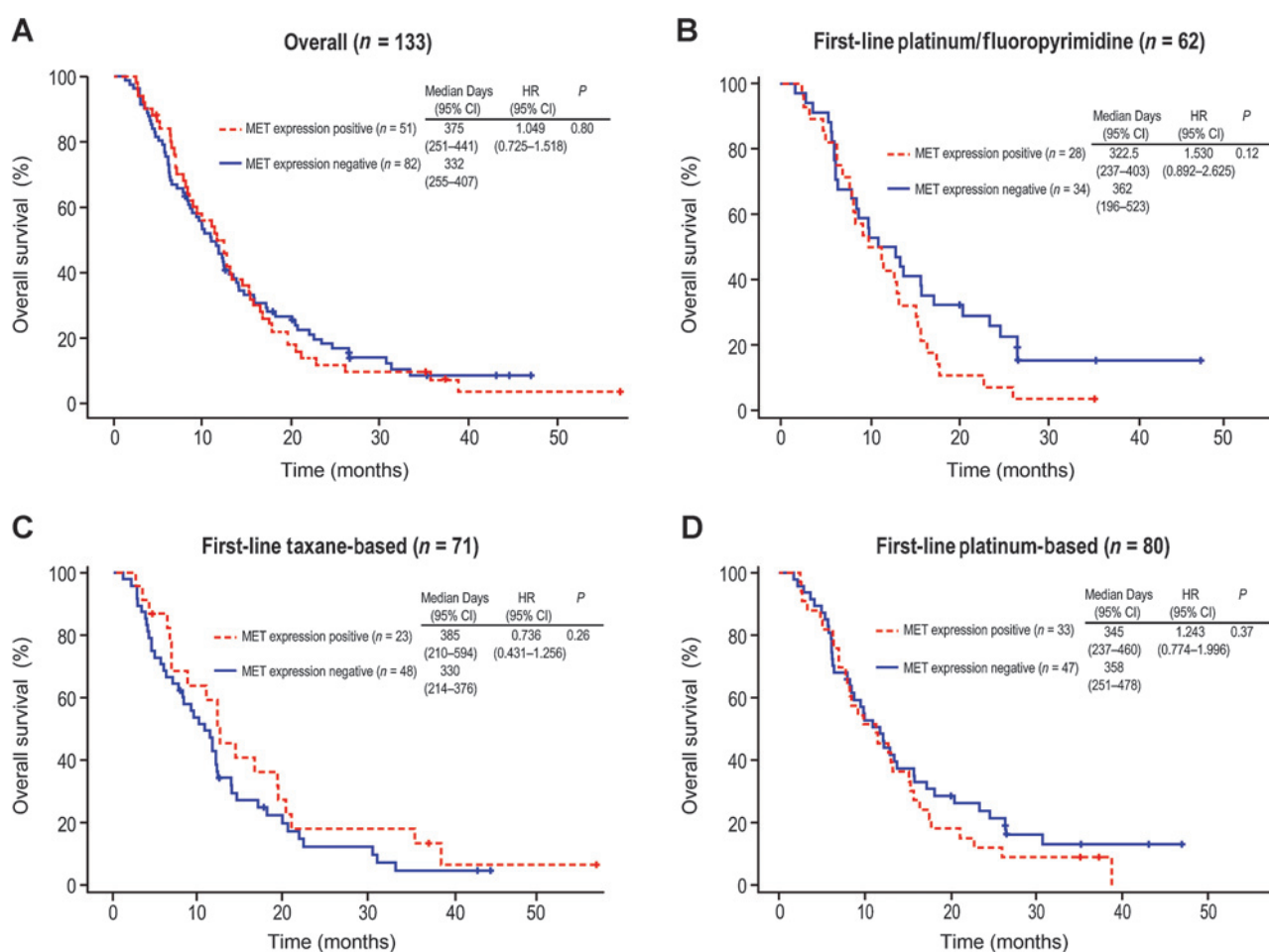
Association between MET expression/MET amplification and HER2

Seventy patients were evaluable for HER2 status and MET expression. Of these, 12 (17%) were HER2-positive and 58 (83%) were HER2-negative (Table 3). MET expression was not associated with HER2 status ($P = 0.75$). Of the 12 HER2-positive tumors, 6 (50%) showed MET-positive expression.

Forty-four patients were evaluable for HER2 status and MET amplification. Of these, 11 (25%) were HER2-positive and 33 (75%) were HER2-negative; no HER2-positive tumors were MET amplified (Table 3). Likewise, no association was observed between MET amplification and HER2 status ($P = 0.56$).

Discussion

To our knowledge, this study is the first to evaluate MET protein expression and MET gene amplification in biopsy samples from Asian patients with advanced gastric or gastroesophageal junction cancer by the MET4 IHC IOU and MET/CEN-7 IQFISH Probe Mix RUO assays. To date, most studies in Chinese patients have employed small sample sizes with patients of variable baseline characteristics (23–25). Our study included 155 patients with available tumor samples, of whom 137 patients were evaluable for MET IHC, and 113 patients were evaluable for MET FISH, all with advanced cancer. Currently, there is no globally recognized standard testing platform for MET. Interpretation of IHC results across studies is hindered by lack of uniform scoring criteria for the different IHC testing methods or MET FISH (14). Recent studies have evaluated MET expression by the Ventana assay (12, 14, 16, 26–29), with MET-positive expression defined as IHC 3+ or 2+ staining in variable percentages of tumor cells. Our study showed a MET-positive expression prevalence rate of 39% by IHC in biopsy samples from Chinese advanced gastric or gastroesophageal junction patients when MET-positive expression was defined as $\geq 25\%$ tumor cells with membrane protein staining at any intensity using the MET4 antibody.

**Figure 3.**

OS of MET expression-positive patients versus MET expression-negative patients. MET expression-positive was defined as $\geq 25\%$ of tumor cells with membrane staining at any intensity. A, in all patients who had a follow-up date or death date and MET status ($n = 133$), no statistically significant difference in OS was observed between the MET expression-positive and MET expression-negative patients ($P = 0.80$). B, in patients receiving first-line platinum/fluoropyrimidine without taxanes ($n = 62$), there was a nonsignificant trend toward shorter OS in the MET expression-positive patients versus MET expression-negative patients ($P = 0.12$). C, in patients receiving first-line taxane-based therapy with or without platinum ($n = 71$), no statistically significant difference in OS was observed between the MET expression-positive patients and MET expression-negative patients ($P = 0.26$). D, in patients receiving first-line platinum-based regimens with or without taxanes ($n = 80$), no statistically significant difference in OS and no apparent trends were observed between the MET expression-positive and MET expression-negative patients ($P = 0.37$).

For the HGF/MET pathway, gene amplification may be a crucial biomarker for MET-targeted agents, especially for small-molecule MET inhibitors. The prevalence of *MET* amplification in gastric and gastroesophageal junction cancer has been reported in several studies by different methodologies, including Southern blot analysis, quantitative PCR (qPCR), and *in situ* hybridization (ISH) technologies [FISH or silver ISH (SISH); refs. 12–14, 16, 26–32]. Earlier studies using Southern blot analysis or qPCR reported relatively high rates of *MET* amplification of approximately 10% (13, 30, 31), but recent studies using FISH or SISH found that *MET* amplification rates were lower, varying from 2% to 8% (12, 26, 27, 29, 31, 32). In our study, the *MET* amplification rate was 7%, which is consistent with the 8% rate reported by An and colleagues who evaluated Chinese patients with locally advanced or metastatic gastric or gastroesophageal junction cancer using a similar FISH method (12). The prevalence of *MET* amplification may be related to

disease stage; our *MET* amplification rate (7%) and that reported by An and colleagues (8%) are relatively high compared with other studies in which the majority of patients had stage I–III disease. For example, a large cohort study by Lee and colleagues, with only 12% of patients having stage IV disease, found *MET* amplification by SISH in 13 of 381 patients (3%) (26). However, in the same study, *MET* amplification was observed in four of 41 patients with stage IV disease (10%). Recent studies of AMG 337, INC280, and crizotinib have shown promising tumor response in *MET*-amplified gastric or non-small cell lung cancers (33–35).

A notable finding of our study was the strong association between MET-positive expression and *MET* amplification in the biopsy tumor samples ($P < 0.001$), consistent with other studies (12, 26). In the small number of samples with *MET* amplification ($n = 8$), all had $\geq 90\%$ MET expression. Furthermore, all samples with $\geq 90\%$ MET expression and

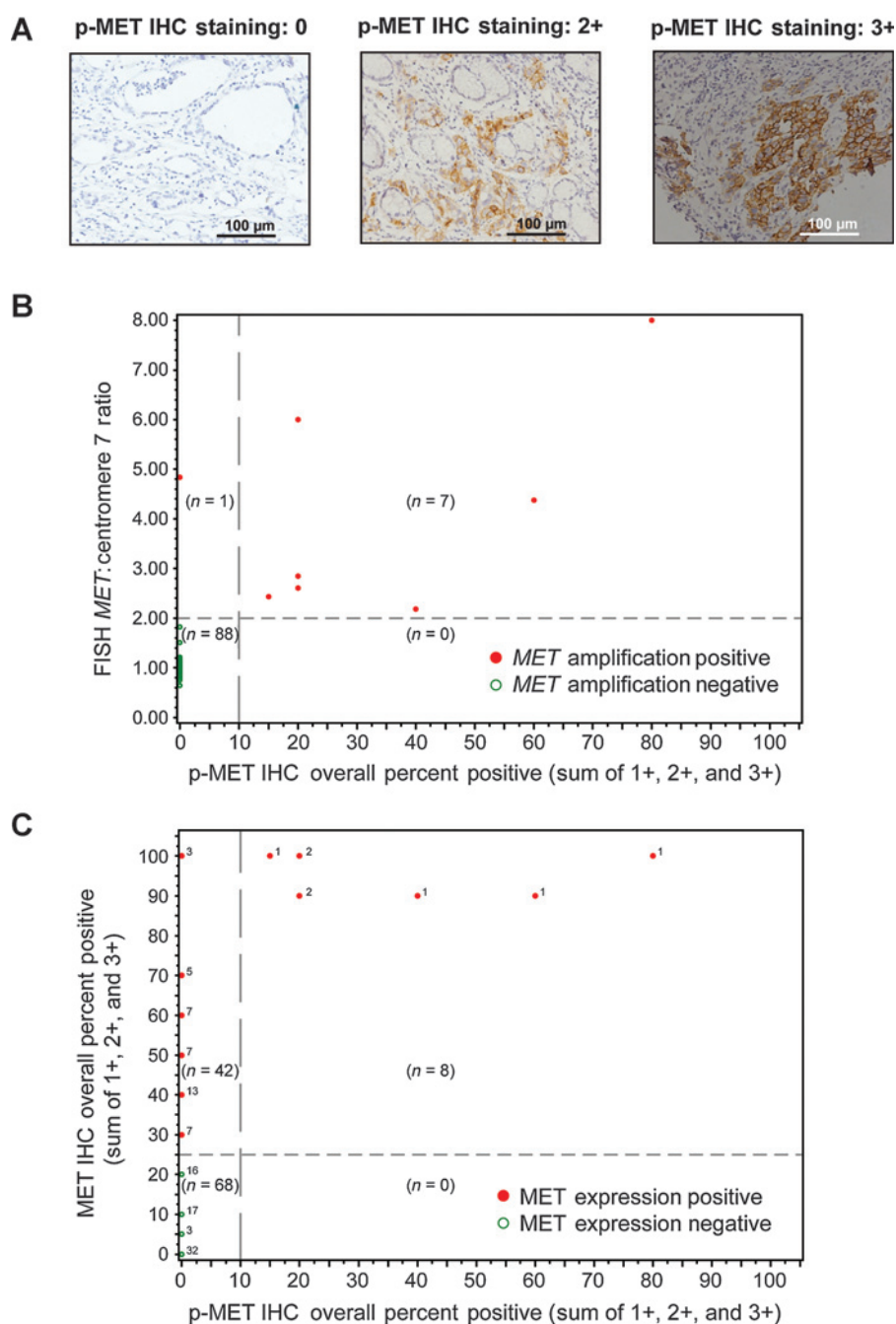


Figure 4. Phospho-MET results. A, representative p-MET immunohistochemistry staining images. B, scatter plot indicating p-MET IHC overall percent positive versus FISH *MET*:centromere 7 ratio ($n = 96$). There was a significant association between p-MET expression and *MET* amplification ($P < 0.001$). C, scatter plot indicating p-MET IHC overall percent positive versus MET IHC overall percent positive ($n = 118$). There was a significant association between p-MET expression and MET expression ($P < 0.001$). Numbers indicate the number of patients represented at each data point.

valid FISH results showed *MET* amplification, except one. However, the number of *MET*-amplified samples is too small to draw strong conclusions. As *MET* amplification may be an important biomarker for MET-targeted agents, it is crucial to find a convenient and cost-effective approach to detect *MET* amplification. Further research is needed to investigate whether IHC may act as a potential prescreening method for *MET* amplification.

We further evaluated p-MET protein expression and the association between p-MET IHC and *MET* FISH. Phospho-MET expression indicates activation of the MET pathway. Therefore, inhibiting the MET pathway in patients with positive p-MET

expression might be a viable therapeutic approach. Moreover, p-MET staining is more convenient compared with *MET* FISH and may act as a substitute method for choosing patients for anti-MET treatment. To date, several studies have evaluated p-MET expression in gastric cancer (36–39), and the results were inconsistent. The p-MET-positive rate of 6% (8/134) observed in our study is similar to the rate reported by Janjigian and colleagues, who also used the same antibody that recognizes p-MET at Y1234/1235 (37). Of interest, we found that there was a strong association between p-MET expression (IHC) and *MET* amplification (FISH). All p-MET-positive samples with valid FISH results showed

Table 2. p-MET IHC results in the *MET*-amplified patients^a

Patient	p-MET IHC status	IHC score	<i>MET</i> :centromere 7 ratio
1	Positive	100	2.85
2	Positive	90	2.18
3	Negative	100	4.84
4	Positive	90	2.60
5 ^b	Positive	100	6
6	Positive	90	4.38
7 ^b	Positive	100	8
8	Positive	100	2.43

^aValid results for both p-MET IHC and *MET* FISH were available for 96 samples.

^b*MET*:centromere 7 ratios for patients 5 and 7 were imputed to 6 and 8, respectively, due to the clustering of FISH signals.

MET amplification, and all samples with *MET* amplification had valid p-MET results and were p-MET positive, except one. To our knowledge, we are the first to show the potentially strong association between p-MET IHC and FISH in patients with advanced gastric or gastroesophageal junction cancer. More studies are needed to confirm whether p-MET IHC may be an alternative and cost-effective method to FISH to select *MET*-amplified patients as a prescreening tool.

In the current study, no significant association was found between *MET* expression and survival, a result that is inconsistent with observations reported by others that patients with *MET*-positive gastric cancer have poorer outcomes than those with *MET*-negative disease (14, 21). When we evaluated OS by different treatment subgroups, there was a nonsignificant trend toward shorter OS for *MET*-positive patients versus *MET*-negative patients receiving first-line platinum/fluoropyrimidine therapy ($n = 62$; 10.6 months vs. 11.9 months, $P = 0.12$).

We did not observe a significant association between *HER2* status and *MET* amplification in our study, which is consistent with other studies (40). Of note, among the 44 patients with samples evaluable for both *HER2* status and *MET* amplification, all four *MET*-amplified samples were *HER2* negative. Our interpretation of this finding is limited by the small sample size, but alteration of either one of these genes may be sufficient to support tumor growth.

In our study, *MET* amplification but not *MET* expression was associated with Lauren classification. A majority of *MET*-amplified samples (seven of eight, 88%) were found in patients with diffuse gastric cancer according to the Lauren classification. These results do not align with the *HER2*-positive status, which is found predominantly in tumors of intestinal classification (2, 41). The difference in Lauren classification between *HER2*-positive tumors and *MET*-amplified tumors provides early evidence that these two tumor types may represent different molecular subtypes.

Table 3. Association between *HER2* status and *MET* expression/*MET* amplification

	Total	<i>HER2</i> ⁺	<i>HER2</i> ⁻	<i>P</i> ^a
<i>MET</i> expression, <i>n</i>	70	12	58	
<i>MET</i> positive, <i>n</i> (%)	30 (43)	6 (50)	24 (41)	0.75
<i>MET</i> negative, <i>n</i> (%)	40 (57)	6 (50)	34 (59)	
<i>MET</i> amplification, <i>n</i>	44	11	33	
Yes, <i>n</i> (%)	4 (9)	0 (0)	4 (12)	0.56
No, <i>n</i> (%)	40 (91)	11 (100)	29 (88)	

^aFisher exact test.

Several limitations of this study should be noted. This was a retrospective study, and the sample size was small, especially in the subgroups. Tumor biopsy samples were not available for all eligible patients, and all samples were not evaluable for IHC and/or FISH. Moreover, the study was limited by the variable first-line treatments among patients. Conclusions regarding outcomes based on *MET* expression may be confounded by differences in subsequent therapies and selection bias for patients with available samples.

Conclusion

In our study, no statistically significant survival difference was observed between the *MET*-positive and *MET*-negative populations, based on *MET* protein expression, in Chinese patients with advanced gastric or gastroesophageal junction cancer. A significant association was found between *MET* gene amplification and *MET* protein expression as well as between *MET* gene amplification and p-MET protein expression. Prospective and larger studies where patients receive uniform treatment are needed to further evaluate potential prognostic markers in Chinese patients with advanced gastric or gastroesophageal junction cancer.

Disclosure of Potential Conflicts of Interest

K.S. Oliner has ownership interest (including patents) in Amgen, Inc. No potential conflicts of interest were disclosed by the other authors.

Authors' Contributions

Conception and design: Z. Peng, J. Gao, K.S. Oliner, Y.-J. Hei, L. Shen
Development of methodology: Z. Peng, K.S. Oliner
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): Z. Peng, Z. Li, J. Gao, M. Lu, J. Gong, K.S. Oliner, L. Shen
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): Z. Peng, J. Gao, M. Liu, E.-T. Tang, J. Gong, K.S. Oliner, Y.-J. Hei
Writing, review, and/or revision of the manuscript: Z. Peng, Z. Li, J. Gao, M. Lu, J. Gong, E.-T. Tang, K.S. Oliner, Y.-J. Hei, H. Zhou, L. Shen
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): Z. Peng, Z. Li, J. Gao, M. Lu, J. Gong, E.-T. Tang, L. Shen
Study supervision: Z. Peng

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