Evaluation of tumor MET and HER2 expression in primary and metastatic gastric or gastroesophageal junction (G/GEJ) cancer

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BACKGROUND: Gastric cancer causes >325,000 deaths in China each year and is a disease with high unmet medical needs. MET and HER-2 are two promising biomarkers for target therapy in advanced gastric or gastroesophageal (G/GEJ) cancer. A better understanding of the expression difference of MET and HER between primary and metastatic lesions would be helpful for us to pick up candidate patients for the target therapy.

EXPERIMENTAL DESIGN: Paired (primary and metastatic) baseline tumor biopsy samples (formalin-fixed, paraffin-embedded) from patients with stage IV unresectable G/GEJ cancer archived at Sun Yat-Sen University Cancer Center (Guangzhou, China) were assessed for MET protein levels and MET gene copy numbers by immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH), respectively. MET-positive: membrane protein staining in ≥25% or ≥50% of tumor cells. HER2 expression was detected by IHC. We evaluated associations between Kaplan-Meier OS and MET status (log-rank test). Expression difference between primary and metastatic lesions were analyzed by Fisher's Exact test. Statistical significance was set at two-sided $P < 0.05$. Study approval was obtained from independent ethics committees at Cancer Center of Sun Yat-Sen University.

RESULTS: 65 patients had paired samples for IHC detection of MET and 55 patients had evaluable FISH samples. The number of paired patients who received IHC detection for HER2 was 44. MET high expression rates were 27.7% and 30.8% for primary and metastatic sites, respectively based on 25% cutoff, P =0.0145. It was 18.5% and 23.1% for primary and metastatic sites, respectively, based on 50% cutoffs, P=0.0004. Of 55 patients with evaluable FISH samples, 6 (10.9%) metastatic sites and 3 (5.5%) primary sites had MET gene amplification, P=0.0008. HER2 positive rate was 20.5% and 15.9% for primary and metastatic sites, respectively, P=0.1876. OS by different levels of MET high expression was shown in the Table.

CONCLUSIONS: MET-positive expression status was significantly higher in the metastatic sites than the primary sites in both IHC and FISH test. While no difference was found for the HER2 expression in primary and metastatic sites. Cutoff 50% was a more powerful cutoff to detect the survival difference between MET positive and negative patients. The expression difference between primary and metastatic sites indicated that we had to test both primary and metastatic sites to explore candidate patients for target therapy.

		Primary sites			Metastatic sites		
HER2	IHC	HER2 – N=35	HER2 + N=9	P[a] values	HER2 – N=37	HER2 + N=7	P[a] values
		427 days [234, 481]	445 [17, .]	0.6943	427 days [289, 509]	445 [92, 560]	0.9311
MET	IHC Cutoff=25 %	IHC+ N=18	IHC- N=47	0.1775	IHC+ N=20	IHC- N=45	0.1616
		324 days [122, 460]	430 [289, 510]		324 days [121, 460]	440 [345, 520]	

	IHC Cutoff=50 %	IHC+ N=12	IHC- N=53	0.0278	IHC+ N=15	IHC- N=50	0.0021
		232 days [91, 460]	440 [392, 509]		167 days [91, 457]	440 [392, 520]	

[a]From log-rank test.