Her2 expression and amplification occurs in a significant subset of gastro-esophageal carcinomas. Her2 is a client protein of molecular chaperones, e.g. heat shock protein (HSP) 90, rendering targeted therapies against Her2/HSP90 an interesting approach. This study aimed to investigate the role and relationship of Her2 and HSP90 in gastric and gastro-esophageal adenocarcinomas. Immunohistochemical determination of HSP90 and Her2 expression was performed on 347 primary resected tumors. Her2 amplification was additionally determined by fluorescence in situ hybridization for all cases. Expression and amplification results were correlated with pathologic parameters (UICC pTNM category, tumor grading) and survival. Elevated Her2 copy numbers were observed in 87 tumors, 21 of them showing amplification. 174 tumors showed Her2 immunoreactivity/expression. HSP 90 immunoreactivity was found in 125 tumors. There was no difference between gastric carcinomas and carcinomas of the gastroesophageal junction regarding Her2 or HSP90. Both high HSP90 and Her2 expression/amplification were associated with earlier tumor stages (p<0.01), absence of lymph node metastases (p<0.02) and Lauren's intestinal type (p<0.001). HSP90 correlated with Her2 expression and amplification (p<0.001 each). Expressions of HSP90 and Her2, but
not Her2 amplification were associated with better prognosis (p=0.02; p=0.004; p=0.802). Moreover, Her2 expression was an independent prognostic factor for overall survival in the subgroup of gastric carcinoma patients (p=0.014) besides pT category, pN category and distant metastases. Her2 expression and gene amplification occurred in a significant subset of cases. Our results suggest a favorable prognostic impact of Her2 expression. This warrants further investigations regarding the significance of Her2 non-amplified tumors showing Her2 immunoreactivity and the definition of Her2 status in gastric cancers. Moreover, the correlation of Her2 expression with the expression of Her2 chaperoning HSP90 may indicate a synergistic regulation. Targeting HSP90 with or without Her2 may offer additional therapeutic options for gastric carcinoma treatment.

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