gastrointestinal tumours, non-colorectal

**EGFR AND AKT1 OVEREXPRESSION ARE MUTUALLY EXCLUSIVE AND ASSOCIATED WITH A POOR SURVIVAL IN RESECTED ADENOCARCINOMAS OF THE STOMACH AND GASTRO-ESOPHAGEAL JUNCTION**

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**Aim:** Trastuzumab is effective for the treatment of advanced gastric cancers with HER2 amplification. Beside HER2 amplification, several molecular targets are under evaluation in metastatic gastric tumors. We evaluated the role of HER2, EGFR, MET, AKT1 and phospho-mTOR expression in resected stage II-III adenocarcinomas.

**Methods:** 92 patients with resected stomach (63%) or gastro-esophageal adenocarcinomas (27%) were evaluated using immunohistochemistry. Antibodies anti-HER2, EGFR, MET, AKT1 and phospho-mTOR were used for immunostaining of formalin-fixed paraffin-embedded tumors slides. Using FISH, HER2 amplification was evaluated in cases with a 2+ staining.

**Results:** EGFR overexpression (11%) was a poor prognostic factor for overall survival (3-year OS: 47% vs 77%; Log-Rank p = 0.033). MET overexpression (36%) was associated with a trend for a worse survival (3-year OS: 65% vs 77%; Log-Rank p = 0.084). HER2 amplification/overexpression and mTOR hyper-phosphorylation were observed in 13% and 48% of tumors, respectively. AKT1 overexpression (8%) was mutually exclusive with that of EGFR and together defined a subgroup of tumors with a poor prognosis (3-year OS: 52% vs. 79%, Log-Rank p = 0.005).

**Conclusions:** EGFR was confirmed a poor prognostic factor in resected gastric cancers. We firstly describe a mutually exclusive overexpression of EGFR and AKT1 with potential prognostic implications, suggesting the relevance of this pathway for the growth of gastric cancers.

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