gastrointestinal tumours, non-colorectal

PROGNOSTIC IMPACT OF HER2, EGFR, AND C-MET STATUS ON OVERALL SURVIVAL OF ADVANCED GASTRIC CANCER PATIENTS TREATED WITH STANDARD CHEMOTHERAPY WITHOUT TRASTUZUMAB IN A FIRST-LINE TREATMENT: A JAPANESE MULTICENTER COLLABORATIVE RETROSPECTIVE STUDY


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Aim: Trastuzumab is the 1st molecular targeting drug that has been shown to confer overall survival benefit adding to chemotherapy in HER2-positive advanced gastric cancer (AGC). Although HER2, EGFR and c-MET have been extensively investigated, these prognostic impact on overall survival (OS) in AGC patients treated with standard chemotherapy without trastuzumab for first-line treatment remains controversial. This study was conducted to investigate the correlation of HER2, EGFR and c-Met status with prognosis, and clinicopathological features in AGC patients who received standard chemotherapy.

Methods: A total of 293 AGC patients from 9 institutes with histologically confirmed adenocarcinoma treated with S-1 plus cisplatin as first-line chemotherapy were eligible. HER2, EGFR, and c-MET were evaluated by immunohistochemistry (IHC) using formalin-fixed paraffin-embedded tumor samples. Additionally, gene amplification was examined using fluorescent in situ hybridization (FISH) for HER2. Positivity was defined as IHC 3+ or IHC 2+ /FISH+ for HER2 and IHC 2+ or 3+ for both EGFR and c-MET.

Results: Among the 293 patients analyzed, 43 (15%) were HER2-positive, 79 (27%) were EGFR-positive and 120 (41%) were c-MET-positive. Only 10 (3%) patients showed positive co-expression for all three molecules. Median follow-up time was 58.4 months with 280 death events. There was no significant difference in OS in terms of HER2 and EGFR status. However, there was a significant difference in OS between c-MET-positive and c-MET-negative patients (median, 11.9 vs. 14.2 months; hazard ratio, 1.31 [95% confidence interval (CI), 1.03–1.67]; log-rank P = 0.024). Multivariate analysis also showed that c-MET-positivity was still a prognostic factor for OS (hazard ratio, 1.32 [95% CI, 1.02–1.69]; P = 0.033).

Conclusions: The present study suggested that c-MET-positive AGC patients had a poorer prognosis than c-Met-negative patients, and that HER2 and EGFR status had no prognostic value in terms of OS in AGC patients treated with conventional chemotherapy as a first-line treatment.

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