A JAPANESE SUBGROUP ANALYSIS OF THE LAPATINIB FOR GASTRIC CANCER (TYTAN) STUDY

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Background: TyTAN is a randomized, open-label, phase III study to evaluate lapatinib (L) plus paclitaxel (P) in the second line treatment in Asian patients (pts) with HER2 amplified (HER2+) advanced gastric cancer (AGC), which did not meet its primary endpoint of overall survival (OS) [Bang, ASCO-GI 2013]. Remarkable regional differences in outcome between 100 Japanese and 161 other pts enrolled were observed in this study; less survival advantage by L (HR 1.09 vs 0.74) and longer OS (median 12.0 vs 10.6 months) in Japanese pts than other pts. To clarify the reasons of outcome differences and whether biology of Japanese pts is different or not, a subgroup analysis was conducted.

Methods: Eligibility of this study had included AGC patients with one prior regimen composed of fluoropyrimidines and/or cisplatin and HER2 amplification by fluorescence in situ hybridization (FISH). Immunohistochemistry (IHC) for HER2 was evaluated at the central laboratory not used for the eligibility but for prescribed subgroup analysis. We conducted a comparative analysis in HER2 status and prior / post treatment statuses between Japanese and other pts.

Results: With respect to HER2 status, pts with IHC 3+ were remarkably less in Japanese than in other pts (42% vs 62%), which might be caused by the presence/absence of local institutional prescreening system between Japan and other countries. Despite the differences, Japanese pts with IHC 3+ showed similar trend of efficacy to ITT population in favor of L group. Remarkable differences in pts background were also seen; more pts with prior history of FU monotherapy in Japanese than other pts (38% vs 16%). Since the enrollment was started from 2008, the former half enrollment period was the time before S-1 + cisplatin was established as the standard of care in Japanese guideline. In addition, post treatment chemotherapy was more frequently administered in Japanese pts, which might cause longer post-progression survival.

Conclusions: This subgroup analysis showed differences in patient background and prior/post treatment statuses between Japanese and other pts, which might affect the regional outcome differences in the TyTAN study.