LBA75 Neoadjuvant chemoradiotherapy followed by surgery versus active surveillance for oesophageal cancer (SANO-trial): A phase-III stepped-wedge cluster randomised trial

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Background: One-third of patients with oesophageal cancer has a pathologically complete response after neoadjuvant chemoradiotherapy (nCRT) plus oesophagectomy. Active surveillance may be an alternative for patients with clinically complete response (CCR).

Methods: A noninferiority stepped-wedge cluster randomised trial was performed. Patients with CCR (*i.e.* no residual disease 6 and 12 weeks after nCRT) underwent active surveillance (surgery only when locoregional regrowth was detected) or standard surgery. Primary endpoint was overall survival (OS) from day of CCR. Noninferiority was defined as Hazard Ratio (HR) <1.77 for mortality in active surveillance after two years. Secondary endpoints were operative outcomes, disease-free survival (DFS), distant dissemination rate and quality of life (HRQOL, EORTC QLQ-C30).

Results: Some 198 patients underwent active surveillance and 111 patients underwent standard surgery. Median follow-up was 34 months in active surveillance and 50 months in standard surgery. OS in active surveillance was noninferior to standard surgery (HR 0.88, 95% upper boundary 1.40, p = 0.007). During active surveillance, 69 patients (35%) maintained CCR, 96 patients (48%) developed locoregional regrowths, and 33 patients (17%) developed distant metastases. R1 rate was 2% in both groups and postoperative 90-day mortality was 4% (active surveillance) versus 5% (standard surgery). Median DFS for active surveillance was 35 (95% CI 31 — 41) versus 49 months (95% CI 38 — NA) for standard surgery (HR 1.35, 95% CI 0.89 — 2.03, p = 0.15). At 30 months after nCRT, 43% of patients with active surveillance versus 34% with standard surgery developed distant metastases (OR 1.45, 95% CI 0.85 — 2.48, p = 0.18). HRQOL was statistically significantly better at six (p = 0.002) and nine months (p = 0.007) for active surveillance.

Conclusions: After a follow-up of two years, patients undergoing active surveillance had noninferior OS and improved short-term HRQOL compared to standard surgery. Postponed esophagectomy for locoregional regrowth was safe. Extended follow-up is required to assess long-term efficacy of active surveillance.

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LBA76 The primary results of an intergroup phase III randomized controlled trial comparing ramucirumab plus irinotecan with irinotecan in the third or later line treatment beyond progression after ramucirumab for advanced gastric cancer (RINDBeRG trial)

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Background: Ramucirumab is a monoclonal antibody that targets the vascular endothelial growth factor receptor 2 (VEGFR-2) and has been shown to improve survival of patients with advanced gastric cancer. It has been reported that sustained VEGF blockade beyond progression had a survival benefit in various cancers.

Methods: This is a multicenter, open-label, randomized phase III study that enrolled patients with unresectable gastric cancer who had received previously ramucirumab containing chemotherapy. Patients were randomly allocated to either irinotecan plus ramucirumab arm or irinotecan alone arm in a 1:1 ratio. Irinotecan was administered at a dose of 150 mg/m^2, every two weeks, in both arms, and ramucirumab at a dose of 8 mg/kg was added biweekly. The primary endpoint was overall survival (OS), expecting a hazard ratio (HR) of 0.77 (a power of 80% with significance level of one-sided 0.05) for full analysis set (FAS). Secondary endpoints include progression-free survival (PFS), overall response rate (ORR), and safety.

Results: From February 2019 to August 2022, 402 patients from 121 institutions participating 9 Japanese clinical trial groups were recruited. As of the data cutoff, 362 events for OS were observed. Median OS in the combination of irinotecan plus ramucirumab and irinotecan alone were 9.4 months and 8.5 months (adjusted HR 0.909, 95% confidence interval [CI] 0.738 — 1.119; p=0.369). Median PFS were 3.8 months and 2.8 months (HR 0.722, 95% CI 0.590 - 0.884; p=0.001) and ORR were 22.1% (33/149) and 15.0% (25/167), respectively. The safety profile was consistent with the known profiles of both irinotecan and ramucirumab, and there were no new safety findings.

Conclusions: This is the first report of the phase III trial to evaluate sustained anti-angiogenic therapy in advanced gastric cancer. In this study, although the addition of ramucirumab to irinotecan after disease progression of ramucirumab improved PFS and ORR with manageable toxicity, the primary endpoint of OS was not met.

Clinical trial identification: This trial was registered at the University Hospital Medical Information Network (UMIN) Clinical Trials Registry as UMIN000023065 from JUL. 13, 2016, and changed to the Japan Registry of Clinical Trials (jRCT) as jRCTs051180187 from Mar. 26, 2019, in accordance with the change of the regulation for clinical research in Japan.

Legal entity responsible for the study: Osaka Gastrointestinal cancer chemotherapy Study Group (OGSG).

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