A randomized phase II trial of S1 plus irinotecan versus S1 plus paclitaxel in advanced gastric cancer as a first-line treatment (OGSG0402).

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Background: S1-based regimens are commonly used for advanced gastric cancer (AGC) in Japan. Both S1 plus irinotecan and S1 plus paclitaxel have shown good overall response rate (ORR) of 48% in respective phase II trial. This randomized phase II trial evaluated these two S1-based regimens in terms of ORR as first-line treatment for AGC to choose the optimal regimen for phase III trial.

Methods: Patients with previously untreated, locally advanced and/or metastatic measurable gastric adenocarcinoma (RECIST), a performance status ≤ 2, and adequate organ functions were randomly assigned to receive S-1 (80 mg/m²/day) for 21 consecutive days plus irinotecan (80 mg/m²) on days 1 and 15, repeated every 5 weeks (SI), or the same dose of S1 for 14 consecutive days plus paclitaxel (50 mg/m²) on days 1 and day 8, repeated every 3 weeks (SP). Both treatments were continued until disease progression or intolerable toxicity occurred. Study endpoints included ORR as primary, progression free survival (PFS), overall survival (OS), and toxicity.

Results: One hundred and two patients were enrolled. Median number of cycles administered was 4 (range, 1-16) for SI, and 4 (range, 1-14) for SP. ORR with confirmed duration of more than 4 weeks was 33.3% (95% CI, 20.8% to 47.9%) for SI arm (n = 51) and 32.0% (95% CI, 19.5% to 46.7%) for SP arm (n = 50). The best ORR was 37.3% (95% CI, 24.1% to 51.9%) for SI arm and 36.0% (95% CI, 22.9% to 50.8%) for SP arm. With the median follow-up duration of X days, median PFS was X and X days for SI and SP, respectively (p=X). The median time to progression (TTP) was X and X days for SI and SP, respectively (p=X). Toxicity was mild, with no treatment-related death. Grade 3/4 neutropenia (SI:20.8%, SP:2.0%), leukocytopenia (SI:6.3%, SP:0.0%), anemia (SI:12.5%, SP:2.0%) and diarrhea (SI:6.3%, SP:2.0%) occurred more frequently in SI arm, while ALT (SI:0.0%,SP:4.0%), AST (SI:0.0%,SP:2.0%) and anorexia (SI:8.0%, SP:8.3%) were more common in SP arm.

Conclusion: This is the first randomized comparison of the two S1-based regimens. Both regimens were active and well tolerated in AGC. No significant difference was found between two arms with respect to ORR. The final analyses of PFS and OS will be presented at the meeting.