gastrointestinal tumours, non-colorectal

A PHASE I STUDY OF GEMCITABINE (GEM), CISPLATIN (CDDP), AND S-1 COMBINATION IN UNTREATED PATIENTS (PTS) WITH ADVANCED BILIARY TRACT CANCER (ABTC)

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Aim: GEM plus CDDP has been established as standard first-line chemotherapy based on the results of the phase III study (ABC-02) in ABTC. An oral FU derivative, S-1 showed a similar activity to GEM in a phase II study and is mainly used in GEM-refractory pts in Japan. To develop a triplet regimen, GEM + CDDP + S-1 (GPS), we assessed its safety in this phase I study.

Methods: The main eligibility criteria were; histologically or cytologically confirmed ABTC, ECOG Performance Status (PS) 0-2, no prior chemotherapy, and written informed consent. Dose limiting toxicities (DLT) were evaluated in following 2 dose levels; GEM (1000 mg/m² at level 1 and 1200 mg/m² at level 2 on day 1) + CDDP (fixed dose of 30 mg/m² on day 1) + S-1 (fixed dose of 40—60 mg/day bid for 7 days), repeated every 2 weeks until progression. The relative dose intensity of GEM and CDDP at level 2 corresponded to 90% of standard GEM plus CDDP regimen. In each level, 6-10 pts were enrolled and assessed. DLTs were evaluated during the first 2 cycles.

Results: Between Oct 2011 and Oct 2013, 18 pts were enrolled and 16 pts were evaluated (median age: 71 years, ECOG PS 0/1: 10/6, intrahepatic/extrahepatic/ gallbladder: 7/3/6). DLTs (grade 3 nausea to stop S-1 in cycle 1 and treatment delay due to grade 3 neutropenia in cycle 2) at level 1 were observed in 2 of the first 6 pts. Additional 4 pts enrolled at this dose level experienced no DLTs. A DLT (G3 anorexia) at level 2 was observed in 1 of 6 pts. Grade 3 or 4 treatment-related adverse events within the first 2 cycles were leukocytopenia (38%), neutropenia (50%), thrombocytopenia (0.6%), nausea (0.6%), and anorexia (0.6%). Of 14 pts with measurable lesions, 7 (50%) pts had partial response and 6 (43%) patients had stable disease. Median progression free survival was 9.2 months (95%CI 6.8-11.6, event in 63%) and overall survival did not reach the median value (event in 38%).

Conclusions: GPS of dose level 2 (GEM 1200 mg/m² and 30 mg/m² on day 1 plus S-1 for 1-7 days, given bi-weekly) was well tolerated, and showed preliminary anti-tumor activity. Further study is warranted. Clinical trial information: UMIN000006123.

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