Phase II Clinical Trial of S-1/Paclitaxel and Cisplatin Triplet Combination Chemotherapy in Patients with Advanced Gastric Cancer

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Introduction: Gastric carcinoma remains a major health problem in many regions of the world. Especially the incidence is extremely high in Korea, but advanced gastric carcinoma remains incurable and patients have a median survival of 6-9 months. Numerous phase II studies demonstrated promising results with newer agents including irinotecan, docetaxel, capecitabine, S-1, and oxaliplatin. The studies on the efficacy and safety of paclitaxel, cisplatin and S-1 in advanced stage stomach cancer with adenocarcinoma in histology are limited. This study were planned to evaluate efficacy, response rate and toxicity in patients with metastatic stomach cancer with triple regimen chemotherapy (paclitaxel, cisplatin and S-1).

Materials & Methods: Eligible patients had untreated metastatic or recurrent stomach cancer with measurable lesion(s), histologic proof of adeno carcinoma, ECOG PS 0-2, adequate organ function, and signed informed consent. Treatment consisted of paclitaxel 80mg/m2 i.v. on day 1, 8, cisplatin 30mg/m2 on day 1, 8 and S-1 35mg/m2 bid p.o. on day 1-14 of 21-day cycle. Measurable and/or unmeasurable lesions were assessed after every 2 courses by RECIST. Primary objectives were to assess the overall tumor response rate. And secondary objectives was to assess progression free survival, the duration of response, time to disease progression, to assess overall survival and to assess the side effect.

Results: From May 2007 to April 2009, total 70 patients (M/F=56/14) were enrolled. The mean age was 55.0 years. The common metastatic lesions were abdominal lymph nodes 52, liver 24, peritoneum 23, pancreas 5 and lung 4. Out of evaluable patients, there were 1 (1.4%) CR, 32 (44.4%) PRs, 14 (19.4%) SDs, and 11 (15.3%) PDs. Objective tumor response was 45.8% in ITT population, Median progression free survival was 5.2 ± 0.6 months, and median overall survival was 10.6 ± 2.8 months. The median cycle number was 4 (range, 1-8). All 70 patients were assessed for safety. This treatment was relatively tolerable with grade 3/4 neutropenia in 19.3%/14.1%, grade 3/4 anemia in 10.2%/1.0%, febrile neutropenia in 8.9% of cycles. Non-hematologic toxicities were grade 2 nausea in 10.0%, grade 2/3 general weakness in 14.3%/4.3%, and grade 2 neuropathy in 5.7% of patients.

Conclusion: For metastatic or advanced gastric carcinoma, definite standard treatment has not been established in the world. Nowadays many countries continue phase II trial containing 5-fluorouracil, leucovorin, irinotecan/cisplatin and TS-1. According to this triplet therapy the overall response rate was 45.8% by the ITT. Objective tumor response was 45.8% in ITT population, Median progression free survival was 5.2 ± 0.6 months, and median overall survival was 10.6 ± 2.8 months. Paclitaxel, cisplatin and S-1 combination chemotherapy showed significant antitumor effect with manageable and tolerable toxicities in patients with metastatic stomach cancer.