Nephrotoxicity of Heptaplatin: A Randomized Comparison with Cisplatin in Advanced Gastric Cancer (AGC)

Jin-Hee Ahn\textsuperscript{1}, Haesong Bahng\textsuperscript{1}, Tae-Won Kim\textsuperscript{1}, Heung-Moon Chang\textsuperscript{1}, Wee-Chang Kang\textsuperscript{3}, Jung-Sik Park\textsuperscript{2}, Jung-Shin Lee\textsuperscript{1}, Woo-Kun Kim\textsuperscript{1}, Sang-Hee Kim\textsuperscript{1}, Yoon-Koo Kang\textsuperscript{1}

Division of \textsuperscript{1}Oncology/Hematology, \textsuperscript{2}Nephrology and \textsuperscript{3}Preventive Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Background Heptaplatin (Sunpla\textsuperscript{8}) is a newly developed cisplatin analogue which was reported to have not only a good activity against AGC but also a favorable toxicity profile comparing with cisplatin. However, we experienced a few cases of severe proteinuria and/or acute renal failure after the widespread use of heptaplatin. This study was designed to evaluate nephrotoxicity of heptaplatin by comparing it with cisplatin in patients with AGC.

Methods Chemotherapy-naive stage IV AGC patients with normal renal function were enrolled in this study. All patients were randomly assigned to receive either SF (Heptaplatin 400 mg/m\textsuperscript{2} 1-hour IV day 1 + 5-FU 1,000 mg/m\textsuperscript{2}/d CIV day 1 to 5), or FP (Cisplatin 60 mg/m\textsuperscript{2} 1-hour IV day 1 + 5-FU 1,000 mg/m\textsuperscript{2}/d CIV day 1 to 5), with the cycles repeated every 4 weeks. A uniform hydration procedure to prevent nephrotoxicity was used in 2 groups. Baseline renal function including 24 hour urinary protein/creatinine excretion ratio (PCR) and serum creatinine (Cr) was measured before the start of first cycle of chemotherapy. Follow-up measurement was done on day 5 of 1st cycle to evaluate acute nephrotoxicity, and before each new cycle to evaluate the long-term effect on renal function.

Results From April 2000 to March 2001, total 92 patients were enrolled; 47 in SF group and 45 in FP group. Baseline characteristics were similar in the 2 groups. When the values of day 5 of 1st cycle were compared with those of pretreatment, urinary PCR increased more in SF group (109±142 mg/g (mean S.D) -> 11305±5393 mg/g) than FP group (100±130 mg/g -> 174±154 mg/g), and serum Cr also increased more in SF group (0.78 ±0.15 mg/dL -> 1.3±0.35 mg/dL) than FP group (0.85±0.19 mg/dL -> 0.95±0.27 mg/dL)(p-value < 0.0001). Significant differences of these parameters were persistent through the cycles between 2 groups (after the end of 4th cycle, PCR 394±471 mg/g vs 102±55 mg/g; Cr 1.15±0.25 mg/dL vs 0.89±0.2 mg/dL). Four cases of acute renal failure developed during the study and they were all in SF group; 1 patients discontinued further cycles of chemotherapy; 3 patients required dose reduction.

Conclusion Our data showed that nephrotoxicity was more severe and durable in patients treated with heptaplatin of 400 mg/m\textsuperscript{2} than cisplatin of 60 mg/m\textsuperscript{2} when it was combined with 5-FU. Measures to prevent nephrotoxicity more effectively should be developed for the safe use of heptaplatin.