Safety and Efficacy of Neoadjuvant Gemcitabine plus Carboplatin Followed by Immediate Cystectomy in Patients with Muscle-Invasive Bladder Cancer: A Propensity Score Analysis

Introduction and Objectives: Standard neoadjuvant chemotherapy has not yet been established for patients with muscle-invasive bladder cancer. Our pervious phase II trial demonstrated the efficacy and safety of neoadjuvant gemcitabine plus carboplatin (GCarbo) chemotherapy followed by immediate cystectomy in patients with muscle-invasive bladder cancer. In the present study, we conducted a propensity score analysis to elucidate clinical significance of the present treatment protocol.
Materials and Methods: The cohort of neoadjuvant group consists of 120 patients with muscle-invasive bladder cancer. They received 2 courses of GCarbo therapy consisting of 800 mg/m^2 gemcitabine on days 1, 8, and 15 and carboplatin with an AUC of 4 on day 2 between March 2005 and June 2011. After the chemotherapy, radical cystectomy (RC) and bilateral pelvic lymph node dissection (PLND) were performed at an interval of 1 month. The cohort of RC alone group includes 155 patients with muscle-invasive bladder cancer treated with RC and bilateral PLND between May 1994 and December 2004. Propensity score matching was used to adjust for potential selection biases associated with treatment type. The endpoints were Overall (OS) and disease-free survival (DFS).
Results: Of the 120 patients who received GCarbo and RC, 28 (23.3%) RC specimens showed pT0. The mean interval from the time of diagnosis of muscle-invasive bladder cancer to RC was 61 days (range 44–99 days). Grade 3/4 neutropenia occurred in 40 patients (33.9%) and thrombocytopenia in 23 patients (19.8%). Propensity score-matched analysis indicated 112 matched pairs from both groups. The median follow-up period was 35.9 months. The 5-year OS rate was 91.5% for neoadjuvant GCarbo versus 51.3% for RC alone group ($P < 0.0001$). The DFS rate was 83.8% for neoadjuvant GCarbo versus 53.1% for RC alone ($P < 0.0001$). Multivariate analysis revealed that the neoadjuvant GCarbo regimen was an extremely strong predictor of the improvement in OS and DFS.
Conclusions: Although the present study is not randomized, neoadjuvant GCarbo therapy followed by immediate RC achieved significantly longer OS and DFS comparing to surgery alone. The clinical usefulness of the present treatment for the patient with muscle-invasive bladder cancer should be verified by further trials.