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Phase II Study of chemotherapy with gemcitabine and cisplatin followed by chemoradiotherapy with capecitabine for locally advanced pancreatic cancer

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Purpose: 5-FU based chemoradiotherapy (CRT) has been the mainstay of treatment for locally advanced pancreatic cancer (LAPC) for the past decades, but the prognosis of LAPC remains dismal. This phase II study was conducted to evaluate the efficacy and toxicity of induction (IND) chemotherapy with fixed dose rate (FDR) gemcitabine (GEM) and cisplain (CDDP), followed by CRT with capecitabine (CAP) in LAPC. **Methods :** Patients who had pathologically confirmed adenocarcinoma of pancreas, ECOG PS of 0-2, and no prior chemo- or radiotherapy were eligible. Treatment consisted of IND chemotherapy with FDR GEM 1000mg/m2 (D1,8) and CDDP 60mg/m2 (D1) every 3 weeks for 3 cycles. Subsequently, patients without progression received CRT (55.8 Gy over 31 fractions) with concurrent CAP (650mg/m2 twice daily). FDR GEM 1000mg/m2 was given on day 1,8 every 3 weeks for 3 cycles after CRT. Time to progression was the primary endpoint. **Results :** From January 2005 to June 2007, we enrolled 28 patients with LAPC (median age 57, M/F: 16/12, ECOG PS 0/1: 3/25). One patient did not meet inclusion criteria, therefore was excluded from the analysis, 4 patients withdrew consent after 1st and 2nd cycle, and remaining 23 patients completed IND chemotherapy. Three (13%) out of 23 patients achieved partial response during IND chemotherapy. Twenty patients without progression after IND chemotherapy completed CRT with mean radiation dose of 54.4 Gy. Further 6 patients progressed during CRT, while 1 additional patient achieved partial response. As of June 2007, 10 patients died and 22 patients showed tumor progression. The median time to progression was 7.9 months (95% CI: 3.5-12.3) and the median overall survival was 14.9 months (95% CI: 10.3-19.6). Grade III/IV toxicities included neutropenia (44.4%/3.7%), thrombocytopenia (3.7%/0%), and anemia (14.8%/0%) during IND phase. Toxicities were generally mild during CRT phase with grade III neutropenia and diarrhea occurring in one and two patients, respectively. One patient died of neutropenic sepsis after 3rd cycle of IND chemotherapy. **Conclusions :** FDR GEM-CDDP IND chemotherapy followed by CAP-RT and maintenance FDR GEM is well tolerated and exhibit a promising efficacy for treatment of LAPC.

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Outcome of leptomeningeal metastasis (LM) from breast cancer is not affected by tumor receptor subtypes

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Background : Leptomeningeal diseases (LM) from breast cancer are detected in up to 19% of patients with brain metastasis at autopsy and their prognosis is known extremely poor. Recently we reported that survival of patients with brain metastasis differed according to triple-receptor status (PASCO 2007 abstract No.11507), which led subsequent survival analysis in leptomeningeal diseases in correlation with clinical characteristics and intrinsic receptor subtypes. **Method :** Between August 2001 and July 2007, 37 patients were hospitalized with LM from breast cancer at National Cancer Center, Korea. The medical records were reviewed for clinical characteristics, triple-receptor subtypes, and details of intrathecal (IT) or systemic chemotherapy. **Results :** The median age was 44 years (range; 23-62) with a median ECOG PS of 2. By July, 2007, 30 of 37 patients died of disease with a median survival from LM to death of 2.0 months (range; 0.3 to 17.9 mo, 95% CI 1.5 to 2.5 mo). Eighteen (48.6%) patients presented concomitantly with brain parenchymal metastasis (BM), 11 (29.7%) after BM treated and 8 (21.6%) LM only. Median survival was significantly different among these 3 groups (3.1 vs 2.2 vs 1.3 mo, P=0.0227). Tumor intrinsic subtypes were luminal A in 14 (37.8%), luminal B in 7 (18.9%), HER2+/ER- in 5 (13.5%) and triple negative in 11 (29.7%) patients. The survival was not significantly different according to triple-receptor status. Among 31 patients who received IT therapy, receipt of concomitant systemic chemotherapy, subsequent negative conversion of CSF cytology and triple IT chemotherapeutic agentsvs doublet were significant variables for survival by univariate analysis. By multivariate analysis, triplet IT therapy (methotrexate, cytarabine and corticosteroid) compared with doublet (methotrexate±corticosteroid) was a significant factor for survival (3.5 vs 1.5 mo, P = 0.0166). **Conclusion :** Unlike in patients with BM, where specific HER2-targeted therapy was attributed to longer survival in HER2+ disease, survival after LM was not influenced by triple-receptor status.