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Dose escalation with hyperfractionation and concurrent FP chemotherapy in inoperable esophageal cancer

J. Kim[1], J. Park[1], E. Choi[1], S. Ahn[1], S. Lee[1], S. Shin[1], S. Kim[2], S. Park[3], H. Song[4], H. Jung[5]. *[1] Asan Medical Center, Radiation Oncology, Seoul, Korea; [2] Asan Medical Center, Medical Oncology, Seoul, Korea; [3] Asan Medical Center, Thoracic Surgery, Seoul, Korea; [4] Asan Medical Center, Diagnostic Radiology, Seoul, Korea; [5] Asan Medical Center, Gastroenterology, Seoul, Korea*

Background: To evaluate the local control rates, survival rates, patterns of failure, and late complications for unresectable esophageal cancers which were treated with hyperfractionated concurrent chemo-radiotherapy with curative intent.

Material and methods: Eighty-five patients with unresectable esophageal cancers received radiation (6,000 cGy/50 fractions/5 weeks, with or without intraluminal brachytherapy with Ir-192, 9-12 Gy/3-4 fractions at 1 cm from the source) with concurrent chemotherapy (CDDP 60mg/m^2 on D1 and 29, 5FU 1,000 mg/m2 continuous infusion at D2-5, 30-33). Response to treatment was measured at 3 or 4 weeks after completion of radiation. Minimum and median follow-up period of surviving patients were 20 and 52 months, respectively.

Results: All patients successfully completed radiotherapy as prescribed. Seventy-five (88%) had reevaluation after treatment, and major responses rate was 73%, including 7 patients with complete remission. Minimal or no response were found in 18 (24%), and disease progression in 2 patients. Overall and disease free survival rates were 26.2% and 20.7% at 2 years and 15.5% and 14.8% at 5 years, respectively. When we compared the survival rates among the three groups, there was no significant difference; however, patients who received external beam dose of 60 Gy or higher showed improved disease free survival. Brachytherapy did not make any difference in disease free survival. Among the 65 whose failure sites could be identified, the rate of local recurrence or persistent local disease was 50.0% and distant metastasis was 29.3%. Hematologic toxicity of NCI-CTC grade 3 or higher was found in 15 patients (22.1%) during chemotherapy. Late esophageal complication was observed in 28 patients (32.9%) including 8 RTOG grade 3 or higher. But it was not related with brachytherapy (17/50 vs 13/35). Overall treatment related mortality rate was 4.7%.

Conclusion: With external beam dose of 60 Gy or higher, disease free survival rate was increased with simultaneous increase of esophageal complications. Hyperfractionation seemed to be not effective for decreasing late esophageal complications in this dose range.

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Modified capecitabine regimen for advanced/metastatic gastric cancer: Final results from a multicenter phase II trial

K. Kondo[1], K. Chin[2], J. Sakamoto[3], H. Kojima[4], M. Terashima[5], Y. Yamamura[6], T. Tsujinaka[7], I. Hyodo[8]. *[1] Nagoya National Hospital, Dept. of Surgery, Nagoya, Japan; [2] Cancer Institute Hospital, Dept. of Medical Oncology, Tokyo, Japan; [3] Kyoto University Graduate School of Medicine, Dept. of Epidemiological & Clinical Research Information Management, Kyoto, Japan; [4] Aichi Prefectural Hospital, Dept. of Gastroenterological Surgery, Okazaki, Japan; [5] Fukushima Medical University, Dept. of Sugery 1, Fukushima, Japan; [6] Aichi Cancer Center, Dept. of Gastroenterological Surgery, Nagoya, Japan; [7] Osaka National Hospital, Dept. of Surgery, Osaka, Japan; [8] National Shikoku Cancer Center, Dept. of Internal Medicine, Matsuyama, Japan*

Background: Capecitabine (Xeloda®) is a novel, orally administered, tumor-activated fluoropyrimidine carbamate with proven activity as first-line treatment in metastatic colorectal cancer. We performed an open-label, multicenter phase II study to evaluate the efficacy and safety of a modified Japanese capecitabine regimen in chemotherapy naïve patients with advanced/metastatic gastric cancer.

Methods: Patients with histologically documented gastric cancer were treated with capecitabine 828 mg/m^2 administered twice daily for 3 weeks followed by one week of rest. Treatment was repeated every 4 weeks for two or more cycles unless patients developed progressive disease. This 4-weekly intermittent regimen had been identified in a previous Japanese phase I study.

Results: A total of 60 patients were enrolled between Feb 1999 and Apr 2001. Baseline patient characteristics were as follows: male/female, 49/11; median age, 64 years (range 28-74); median treatment duration, 4 cycles (range 1-37). 55 patients were evaluable for response by an independent review committee. The overall response rate was 25.5% (95% CI, 14.7-39.0%), including 4 complete responses and 10 partial responses. A further 16 patients (29.1%) had stable disease. The median time to progression was 3.4 months (95% CI, 1.8-6.1 months) and median overall survival was 10.0 months (95% CI, 6.4-13.5 months). Hand foot syndrome, anorexia, nausea and diarrhea were the most common adverse events. The most frequent (greater than 10% of patients) grade 3/4 adverse event was hand foot syndrome (13.3%). However, no grade 3/4 diarrhea was observed and only 10% of patients developed grade 3/4 hematological toxicity.

Conclusion: This modified capecitabine regimen was convenient, effective, well tolerated and contributed to a long survival time when administered as first-line therapy in patients with advanced/metastatic gastric cancer. Further investigation of this capecitabine regimen as monotherapy and as part of combinations in the metastatic and adjuvant settings is warranted.

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Gastrazole, a novel CCKB/gastrin receptor antagonist, in the treatment of advanced pancreatic cancer: results from two randomised controlled trials

I. Chau[1], D. Cunningham[1], C. Russell[2], A.R. Norman[3], P. Harper[4], P. Harrison[5], P.J. Ross[1], R. Hull[6], M. Walker[6], J. Black[6]. *[1] Royal Marsden Hospital, Department of Medicine, London and Surrey, United Kingdom; [2] The Middlesex Hospital, Hepato-Pancreato-Biliary & Endocrine Surgical Unit, London, United Kingdom; [3] Royal Marsden Hospital, Department of Computing and Information, London and Surrey, United Kingdom; [4] Guy's Hospital, Department of Medical Oncology, London, United Kingdom; [5] King's College Hospital, Institute of Liver Studies, London, United Kingdom; [6] James Black Foundation, London, United Kingdom*

Background and purpose: Gastrin has been shown to be a growth stimulant in pancreatic cancer cells. Gastrazole is a potent and selective gastrin receptor antagonist. In a previous randomised controlled trial for advanced pancreatic cancer, protracted venous infusion (PVI) 5-FU produced 1-year survival rate of 23.5% (Maisey et al JCO 2002) – similar to that achieved with gemcitabine. Two randomised trials were conducted to assess the effect of gastrazole in advanced pancreatic cancer.

Patients and Methods: Patients with biopsy-proven, inoperable pancreatic carcinoma were recruited into both studies. Trial 9902 compared PVI gastrazole (500mg/day) with PVI placebo in a double blinded fashion. Trial 9901 compared PVI gastrazole (500mg/day) with PVI 5-FU (300mg/m2/day) in a single blinded fashion.

Results: Between June 00 and November 02, 18 patients (M:F 13:5) were randomised in trial 9902. The median age of patients was 60 (range: 44-78). 33% of patients had metastatic disease. Gastrazole produced significantly better survival compared to placebo (median 7.8 months vs, 4.5 months; 1-year survival: 38% vs. 11% respectively; log rank p=0.0167). No difference in toxicity was seen between gastrazole and placebo. Between June 99 and November 02, 98 patients (M:F 52:46) were randomised in trial 9901. The median age of patients was 65 (range: 35-82). 59% of patients had metastatic disease. No significant survival difference was detected between gastrazole and 5-FU (median: 3.6 months vs. 4.2 months; 1-year survival: 16.9% vs. 23.9% respectively; log rank p=0.7518). Toxicity of gastrazole was mild with significantly less diarrhoea (p=0.02), stomatitis (p

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Clinical results of proton radiation therapy alone for esophageal cancer

S. Sugahara[1], K. Tokuuye[1,2], T. Okumura[3], A. Nakahara[4], Y. Saida[5], K. Kagei[1,2], K. Ohara[1], S. Hata[1,2], N. Tanaka[4], Y. Akine[1,2]. *[1] Tsukuba University Hospital, Radiation Oncology, Tsukuba, Japan; [2] Tsukuba University, Proton Medical Research Center, Tsukuba, Japan; [3] Central Hospital and Cancer Center of Ibaraki Prefecture, Radiation Oncology, Tomobe, Japan; [4] Tsukuba University Hospital, Internal Medicine, Tsukuba, Japan; [5] Tsukuba University Hospital, Radiology, Tsukuba, Japan*

Background: Proton radiation therapy can deliver higher doses to the target with a considerably smaller dose affecting the adjacent normal tissue when compared to conventional radiotherapy. The aim of this study was to evaluate the clinical results of proton radiation therapy alone for patients with locally confined esophageal cancer.

Methods and Materials: Forty-six esophageal cancer patients who were treated with 250 MeV protons with or without x-rays between 1985 and 1998 were analyzed. All patients had local-regionally confined disease, and had squamous histology except for one adenocarcinoma. The median tumor length was 4.0 cm (range, 1.5-15.0). Forty patients received combinations of x-rays (median 48 Gy) and protons (median 31.7 Gy) over 44 - 99 days (median 61 days) as a boost. The median total dose of combined x-ray and