Results: The median follow-up duration of survivors was 135 (112–176) months. HP(−) was significantly correlated with old age (>54), total gastrectomy, Bormann type IV, larger tumor size (>5 cm), and stage IIIB. In univariate analysis, pts with HP(−) (138 pts) demonstrated significantly poor 10-year OS compared with those with HP(+) (136 pts) (20.9% vs. 82.3%, $p < 0.0001$). HP(−) was associated with poor outcome in all stages. In multivariate analysis, HP(−) was the most significant independent prognostic factor of poor OS (hazard ratio: 6.32, 95% CI: 4.10−9.74, $p < 0.0001$) followed by advanced stage ($p = 0.001$) and old age ($p < 0.0001$).
Conclusions: HP infection status seems to have strong prognostic significance in locally advanced gastric cancer. HP(−) pts may need intensified adjuvant treatment and careful follow-up.

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Phase II study of docetaxel, oxaliplatin and S-1 (DOS) for patients with advanced gastric cancer

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Background: Docetaxel, oxaliplatin and S-1 have shown significant efficacy in gastric cancer. These drugs have distinct mechanisms of action and no overlapped key toxicities. Furthermore, fluoropyrimidine and docetaxel or oxaliplatin have shown synergism in vivo studies and in clinical trials. We performed a phase II study of combination docetaxel, oxaliplatin and S-1 (DOS) to evaluate the efficacy and safety in advanced gastric cancer.
Material and Methods: Eligible patients were those who had unresectable, locally advanced or metastatic, gastric adenocarcinoma. Both initially diagnosed and recurred patients with no previous history of chemotherapy except adjuvant chemotherapy were enrolled. The patients of age 18 to 70 with ECOG PS 0−2 were enrolled to this study. Docetaxel 52.5 mg/m^2 and oxaliplatin 105 mg/m^2 were administered intravenously on day 1 and S-1 80 mg/m^2 was administered orally on days 1−14. Cycles were repeated every 21 days. Patients were treated until disease progression or unacceptable toxicity.
Results: Forty-two patients (male/female 31/11; median age 55, range 25−69; ECOG PS 0/1/2 13/28/1) have been enrolled in this study. Ten patients had recurred cancer after surgery and 32 patients were diagnosed as a metastatic disease. Tumor differentiation was 5 well, 11 moderate, and 26 poor. Main sites of metastasis were 37 lymph node, 18 peritoneum, 11 liver, 1 bone and 9 others. A total of 225 cycles were administered (median 4, range 1−24). Thirty-nine patients were evaluated for toxicity and thirty-seven for response. The common grade 3/4 toxicities were leukopenia (23% of patients), neutropenia (36%), febrile neutropenia (13%), and anemia (10%). There were 2 CR and 19 PR. The overall response rate was 57%. The preliminary median progression free survival was 11.4 (95% CI, 8.1−14.8) months and median survival time was 15.8 (95% CI, 2.1−29.6) months.
Conclusions: These data suggest that DOS regimen is active and is well tolerated in patients with advanced gastric cancer.

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A phase II study of Docetaxel and Oxaliplatin combination as first-line chemotherapy in recurrent gastric cancer patients after Fluoropyrimidine and/or Cisplatin adjuvant treatment

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Background: After two important randomised trials of the East (S-1 as adjuvant treatment; Sakuramoto S et al, N Engl J Med 2007) and the West (MAGIC trial; Cunningham D et al, N Engl J Med 2006), surgery alone is no longer the standard treatment for patients with resectable gastric cancer. Therefore, urgent investigation is demanded which regimen is more effective for patients with recurrent gastric cancer after combined treatment with surgery and perioperative or adjuvant chemotherapy.
Materials and Methods: Patients with histologically confirmed and measurable advanced gastric cancer that had relapsed after fluoropyrimidine and/or cisplatin-based adjuvant chemotherapy received docetaxel 35 mg/m^2 i.v. on day 1, 8 plus oxaliplatin 100 mg/m^2 i.v. on day 1 every 3 weeks until disease progression or unacceptable toxicities.
Results: Between Feb 2007 and Mar 2009, total 27 patients (pts) who had received adjuvant chemotherapy for median 5.7 months (range, 0.1−49.1) were enrolled. A total of 18 pts (66.7%) had exposed all two drugs for fluoropyrimidine and cisplatin. The median age was 58 years (range, 40−68). After a median 4 (range, 1−13; total, 123) cycles of chemotherapy, 25 pts and 120 cycles were evaluable for response and toxicity, respectively. In intention-to-treat analysis, the overall response rate was 44.0% (95% C.I., 24.6−63.4%), including 1 CR, 10 PRs. After a median follow-up of 8.5 months (range, 2.0−20.6), median time to progression was 6.9 months (95% C.I., 3.4−10.4) and median overall survival was 12.8 months (95% C.I., 8.7−16.7). Commonly observed grade 3/4 adverse events were neutropenia (52.2% of pts), diarrhea (20.0%), anorexia (8.0%), stomatitis (8.0%) and motor neuropathy (4.0%). Treatment was delayed in 29 cycles (24.2%). The dose of docetaxel on D1, 8 and oxaliplatin were reduced during 22 (18.3%), 25 (20.8%) and 23 cycles (19.2%), respectively. Major causes for treatment delay and dose reduction of two drugs were neutropenia and diarrhea. There were three pts of neutropenic fever, and one pt of treatment-related death.
Conclusions: Docetaxel and oxaliplatin combination chemotherapy was active and tolerable except grade 3 diarrhea as first-line treatment in patients with recurrent gastric cancer after fluoropyrimidine and/or cisplatin-based adjuvant chemotherapy.

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Characteristics of patients with early gastric cancer who had undergone surgery in two institutes

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Background: The incidence of early gastric cancer (EGC) has been increasing worldwide owing to advances with diagnostic techniques and screening programs. The present study was designed to investigate the characteristics of EGC patients who had undergone surgery.
Materials and Methods: EGC is defined according to the Japanese classification of gastric carcinoma. We reviewed 529 patients with gastric cancer who had undergone gastrectomy at Masan Samsung Hospital, Masan, Korea and Ulsan University Hospital, Ulsan, Korea from December 2002 to December 2005.
Results: Two hundred sixty-one patients (49%) were diagnosed as EGC (155 intramucosal EGC (mEGC), 106 intrasubmucosal EGC (smEGC), 123 differentiated EGC, and 138 undifferentiated EGC). The mean diameter of tumor was 2.49±1.55 cm (2.18±1.45 cm in mEGC and 2.94±1.60 cm in smEGC, $p = 0.000$). The incidence of lymph node metastasis was 11.5% (30 out of 261 patients). Univariate analysis revealed that a tumor larger than 2 cm (17.6% vs. 6.3%), submucosal invasion (20.8% vs. 5.2%), and the presence of lymphovascular invasion (LVI) (33.3% vs. 6.6%) were significantly associated with a higher lymph node metastasis rate. In multivariate analysis, LVI was independent predictive factor for lymph node metastasis ($p = 0.005$), while submucosal invasion was marginally predictive ($p = 0.069$) and tumor size was not ($p = 0.208$). At a median follow-up of 1023 days, only 2 patients relapsed and 1 patient died due to disease progression.
Conclusions: LVI was independent predictive factor for lymph node metastasis. In cases that LVI was present after endoscopic resection, radical gastrectomy should be recommended. Endoscopic resection data will be analyzed and compared with surgery data.

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A phase II study of weekly low-dose docetaxel and oxaliplatin as first-line treatment in patients with advanced gastric cancer

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Background: Docetaxel and oxaliplatin are active agents for advanced gastric cancer. The combination of these two drugs in tri-weekly schedule

is an active and attractive regimen for gastric cancer but with significant hematological toxicities. A multicenter phase II study was designed to establish an active regimen with good tolerability by using weekly docetaxel-oxaliplatin (DO) combination in GC patients.
Materials and Methods: Eligible patients had histologically confirmed stage IV gastric cancer without previous palliative chemotherapy; age $\geqslant$18, ECOG performance status $\leqslant$2, at least one measurable lesion, adequate hematologic, renal and liver functions. All patients received premedications with dexamethasone and 5-HT3 antagonist before chemothearpy. Docetaxel (Taxotere®, sanofi-aventis) 30 mg/m^2 followed by oxaliplatin (Eloxatin®, sanofi-aventis) 65 mg/m^2 were administrated on day 1 and 8 of each 21-day cycle. Treatment continued until disease progression, intolerable toxicity, or consent withdrawal. Toxicities were graded by CTCAE version 3.0. Tumor responses were evaluated every 2 cycles by RECIST criteria.
Results: From May 2007 to December 2008, a total of 47 patients were enrolled. There were 8 females and 39 males with a median age of 57 years old (range 26−76). Forty-three patients were evaluated for response. The complete response was 2 (4.7%), partial response rate was 12 (27.9%), stable disease was 20 (46.5%), and progression disease was 9 (20.9%), respectively. The total response rate was 32.6% (95%CI 19.1−48.5%). The median time to disease progression was 4.2 months and the median time of overall survival was 7 months. All 47 patients were assessable for toxicity. A total of 202 cycles were given in 47 patients with a median cycle of 4 (1−10). Major grade 3/4 hematologic toxicities were anemia (5 patients, 10.6%), leukopenia (2patients, 4.3%), and neutropenia (1 patient, 2.1%). The most common grade 3/4 non-hemtaologic toxicities were fatigue (3 patients, 6.4%) and AST elevation in 3 patients (6.4%).
Conclusions: The combination of weekly DO demonstrated a well tolerable profile with moderate activity in the treatment of advance gastric cancer.

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Adjuvant chemoradiation in stage III-IV radically resected gastric cancer patients: a pilot study

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Objective: Adjuvant chemoradiation (CT-RT) in resected high-risk gastric cancer patients does not represent the standard care but the results from phase II and randomized trials suggest an improvement of overall survival. This study was aimed to determinate feasibility and toxicity of CT (FOLFOX-4) and RT combination as adjuvant treatment in locally advanced gastric cancer.
Patients: Twenty-nine patients (male 24, female 5, median age of 57 year; PS ECOG 0 for 23 patients, PS ECOG 1 for 6 patients) with T_4N_+ or any T N_{2-3} gastric cancer, previously treated with potentially curative surgery were enrolled. All patients received a combined scheme of adjuvant chemotherapy with FOLFOX-4 (Oxaliplatin 85 mg/mq d1, 5-FU 400 mg/mq bolus ev d1−2 and CI 1200 mg/mq ev over 48 hours, Lederfolin 200 mg/mq ev d1−2 every 2 weeks) for a total of 8 cycles, and concomitant RT for a total 45 Gy in 25 daily fractions over 5 weeks. Radiation therapy started after the first 2 cycles of FOLFOX4, with a dose reduction of 80% during the all period of concomitant radiation therapy. Treatment toxicity was assessed according to the NCT-CTC classification. Overall (OS) and progression-free (PFS) survival rates; identification of prognostic indicators of outcome.
Results: All patients completed treatment. Severe hematological and gastrointestinal toxicities were 10% and 33%, respectively. Nor acute hepatic neither renal toxicity was observed; one patient experienced grade 3 neurotoxicity. PFS and OS rates at 1, 2 and 3-year were 79%, 35%, 35%, and 85%, 62.6%, 50.1%, respectively; substantially better than percentages observed in untreated patients. Long-term outcome was related to TNM stage, basal serum tumour marker levels, and, particularly, to the lymph node ratio.
Conclusions: The multimodal approach with FOLFOX4 and radiation is feasible and active for the treatment of high-risk resected gastric cancer patients.

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Toxicity of neoadjuvant intraperitoneal and systemic chemotherapy in gastric cancer with peritoneal dissemination

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Background: Neoadjuvant intraperitoneal and systemic chemotherapy (NIPS) is a new treatment modality in gastric cancer with peritoneal seeding. It was developed to increase the rate of complete cytoreduction of peritoneal carcinomatosis. In 2006 Yonemura et al [1] published the results of a phase II clinical trial with NIPS and cytoreductive surgery with an increase in overall survival in patients who achieved a complete resection compares to historical controls and with an acceptable toxicity. We report the toxicity of the first experience in Spain with NIPS in gastric cancer with peritoneal carcinomatosis.
Materials and Methods: Chemotherapy was delivered through an implantable peritoneal catheter. All patients received the following treatment: docetaxel 40 mg intraperitoneal (ip) and carboplatin 150 mg ip in 30 minutes infusion and methotrexate 100 mg/m^2 intravenous (iv) and 5-fluorouracil 600 mg/m^2 iv both in bolus the same day on a weekly basis. Eleven patients have been enrolled in this protocol in three different spanish centers in a compassionate use program. Five patients received 6 doses, 2 patients 5 doses, 2 patients 4 doses and 2 patients 3 doses. Male/female: 63% vs 37%. Median age: 50.2 years.
Results: The most common adverse event was diarrhoea (81% overall and grade [gr] 3−4 18.2%). Febrile neutropenia gr 3−4 18.2% and thrombocytopenia gr 3−4 9%. No primary prophylaxis with G-CSF was used. Abdominal pain gr 3−4 9% and asthenia gr 3−4 9%. No other gr 3 or 4 toxicities have been described. No treatment-related deaths. One patient discontinued chemotherapy due to toxicity (febrile neutropenia and diarrhoea). There were no complications due to the peritoneal catheter. Late and unexpected toxicities have not been observed.
Conclusions: The first results suggest this regimen is feasible and safe. A longer follow up is needed to define the morbidity and mortality associated to surgery after NIPS. Data from phase III clinical trials are essential to confirm these results and define the optimal use of NIPS.

References

[1] * Yonemura Y, Banou E, Sawa T et al. Neoadjuvant treatment of gastric cancer with peritoneal dissemination. Eur J Surg Oncol. 2006 Aug;32(6):661−5.

6552 POSTER

Phase II study of weekly paclitaxel as thirrd line chemotherapy for advanced or recurrent gastric cancer (Osaka Gastrointestinal Cancer Chemotherapy Study Group: OGSG0602)

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Background: The median survival time was longer than 1 year in randomized phase III studies for advanced or recurrent gastric cancer (GC) recently conducted in Japan. Although progression free survival of first-line chemotherapy has improved, many patients receive for second-line or later therapies with new agents such as paclitaxel or docetaxel after first-line treatment. It may contribute greatly to prolong overall survival. This study evaluated the efficacy and safety of weekly paclitaxel as thirrd line chemotherapy in patients with advanced or recurrent GC.
Material and Methods: The criteria for eligibility were histologically proven advanced or recurrent GC, had given with prior two regimens including S-1 and irinotecan, age $\geqslant$20, performance status (PS) 0−2, adequate organ function, and informed consent received paclitaxel 80 mg/m^2 on day 1, 8 and 15 of a cycle for 4 weeks until progression. Primary endpoint is feasibility and secondary endpoints are safety, overall survival, progression free survival (PFS), time to treatment failure (TTF) and relative dose intensity in this study.