Poster presentations (Wed, 23 Sep, 14:00−17:00)
Gastro-intestinal malignancies − Non-colorectal cancer

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Weekly intravenous and intraperitoneal paclitaxel combined with S-1 for advanced gastric cancer with peritoneal metastasis

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Background: A phase II study to evaluate the efficacy and tolerability of weekly intravenous and intraperitoneal paclitaxel combined with S-1 was performed in gastric cancer patients with peritoneal metastasis.
Methods: Gastric cancer patients with peritoneal dissemination and/or cancer cells on peritoneal cytology were enrolled. Paclitaxel was administered intravenously at 50 mg/m^2 and intraperitoneally at 20 mg/m^2 on days 1 and 8. S-1 was administered at 80 mg/m^2/day for 14 consecutive days, followed by 7 days rest. The primary endpoint was the 1-year overall survival rate. Secondary endpoints were the response rate, efficacy against malignant ascites and safety.
Results: Forty patients were enrolled, including 21 with primary tumors with peritoneal dissemination confirmed by staging laparoscopy, 13 with peritoneal recurrence, and 6 with positive peritoneal cytology only. The median number of courses administered was 7 (range 1−23). The 1-year overall survival rate was 78% (95% CI, 65−90%). The overall response rate was 56% (95% CI, 32−79%) in 18 patients with target lesions. Malignant ascites disappeared or decreased in 13 of 21 (62%) patients. The incidences of grade 3/4 hematological and non-hematological toxicities were 40% and 15%, respectively. The frequent grade 3/4 toxicities included neutropenia (38%), leukopenia (18%), anemia (10%) and nausea (8%). Catheter obstruction observed in one patient was the only complication related to the peritoneal access device or intraperitoneal infusion. There were no treatment-related deaths. Gastrectomy was performed in 16 patients after response to chemotherapy, and the 1-year overall survival rate was 94%.
Conclusions: Combination chemotherapy of intravenous and intraperitoneal paclitaxel with S-1 is well tolerated and active in gastric cancer patients with peritoneal metastasis.

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Analysis of patterns of failure after a study of interobserver variability in target volume delineation in postoperative radiochemotherapy for gastric cancer

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Background and Purpose: In 2001, the INT0116 trial showed that adjuvant chemoradiotherapy has a significant role in reducing recurrence and increasing survival in gastric cancer.
However, a previous study of interobserver variation between radiation oncologists in volume delineation reported a significant difference in standard deviation between observers, although this was clinically less evident (ESTRO 27 #4556). The aim of the present study was to analyze failure patterns by delineated fields and determine if there is a relation with radiation oncologists volume delineated.
Materials and Methods: In 2008, four physicians from our hospital trained in delineating upper abdomen volumes were asked to delimitate the planning target volume (PTV) according to the MacDonald scheme on the same 3D CT-images in 9 postoperative radiochemotherapy gastric cancer cases. Instructions were given to include the tumor bed, the remaining stomach if partial surgery was performed, anastomosis, the duodenal loop and perigastric, celiac, local paraaortic, splenic, hepatoduodenal and pancreaticoduodenal lymph nodes. Enhanced preoperative CT images were available. None of the observers had knowledge of the volumes outlined by the others.
One year later we analyzed the status of these patients by recording recurrences and reviewing the 3D-planning volumes, as either distant or locoregional (gastric or tumor bed, the anastomosis and regional lymph nodes), assuming that PTV included more than group 2 lymph nodes. Any lymph node recurrence outside the PTV was defined as distant metastasis.
Results: The median follow up was 12.3 months (range 6−17 months). At this time 4 patients relapsed. The mean time to relapse was 9.32 months (range 6.23−6.18), and all of them presented distant recurrence while 1 also had locoregional recurrence. Distant metastases were commonly peritoneal seeding, but in two cases extra-abdominal metastases (CNS and lungs) were found. Only one case of locoregional failure and relapse was both within and outside of the PTV in all four delineated volumes. One case was lost of follow up and analysis excluded. Five patients remain free from disease.
Conclusions: Locoregional recurrence rates and patterns of failure correlate to published results. No differences were found between observers in locoregional failure, confirming poor clinical impact of interobserver variation between radiation oncologists in volume delineation as reported in previous study.

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Adjuvant chemoradiotherapy with continious infusion 5-fluorouracil and bi-weekly cisplatin and infusional 5-fluorouracil for operated locally advanced gastric cancer

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Background: Adjuvant chemoradiotherapy followed by surgery for gastric cancer is widely accepted in clinical practice, but optimal regimen is still debated. In this study was analysed the effectiveness and aplicability of adjuvant treatment protocol with cisplatin, infusional 5-fluorouracil (5FU) and folinic acid (CFF) plus infusional 5FU and concurrent radioterapy in patients with gastric adenocarcinoma.
Material and Methods: Between May 2005 and Dec 2008, 65 curatively resected gastric adenocarcinoma were included in this restrospective study. Inclusion criteria were as follows: pathologic tumor category T4, or N2 or N3 or involved/resected lymph nodes with ratio greater than 1/3. Chemotherapy regimen consisted of folinic acid 200 mg/m^2, cisplatin 50 mg/m^2, 5FU 400 mg/m^2 bolus followed by 5FU 1600 mg/m^2 46 h-continuous infusion every 14 days. Chemoradiotherapy was administered after 2 cycles of CFF_{14} (consisting of 4 courses chemotherapy) as a radiotherapy 4500 cGy, 5 weeks and concurrently 5FU 200 mg/m^2/day. Two more cycle of CFF were administered after chemoradiotherapy. The results was compared with those of 62 patients at similiar stages treated in accordance with Intergroup 0116 trial in our clinic.
Results: Of patients, 48 were male and the median age was 55 years. Their clinical stages were stage II in 1 patient, stage III in 37 patients and stage IV M0 in 27 patients. D1 and D2/D3 lymphadenectomy was performed in 21.4% and 78.5% patients, respectively. Fifty seven (87.7%) patients could complete at least 90% of planned treatment. Grade 3/4 hematologic toxicity occured in 16.8% and grade III/IV non-hematologic toxicity occured in 13.7% of patients. The median follow-up for CFF and Intergroups arms was 15 (6−36) months and 15.5 (3−72) months, respectively. While two groups were equal for stage and prognostic parameters, patients with N3 were much more (24 vs 8 patients) in CFF group ($p = 0.002$). Median disease free survival (18 months, 95% CI: 13.9−22.0) was insignicantly ($p = 0.51$) longer in CFF_{14} patients than INT0116 patients (14 months, 95% CI: 7.7−20.3). Median overal survival of CFF_{14} patients (19 months, 95% CI: 15.2−22.8) was almost identical with INT0116 patients (20 months, 95% CI: 12.6−27.3) ($p = 0.73$). However, grade 5 toxicity was much more common in Intergroup arm (0 vs 5 patients, $p = 0.02$).
Conclusion: Bi-weekly CFF_{14} and concurrent radiotherapy protocol seems to be well tolerated (87.7% of patients could receive the whole set) and it provided equivalent survival rates with INT0116 protocol for locally advanced gastric adenocarcinoma patients.

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Palliative chemotherapy does not improve survival in metastatic oesophageal cancer

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Background: The role of chemotherapy in metastatic oesophageal carcinoma (MOEC) remains debated as randomised trials comparing chemotherapy to best supportive care are lacking. The objective of this retrospective study on one of the largest series of MOEC ever reported was to analyse the survival impact of chemotherapy after stratification to prognostic factors (PF).
Material and Methods: All consecutive MOEC treated at the Northern France Cancer Center (Centre Oscar Lambret) from 1995 to 2008 were randomly split into a development ($n = 171$) and a validation cohorts ($n = 113$). We had first identified PF on development cohort and validated then on the validation cohort. Then, we analysed the impact of chemotherapy after stratification to these PF. Of 284 patients, 250 were men, and median age was 59 (range, 37−86). Main metastatic sites

were extra-mediastinal lymph nodes (57%) and lung metastasis (53%). Metastases were synchronous in 151/284 cases (53%) Squamous cell carcinoma accounted for 80% of cases. The dysphagia score was graded 3 or 4 in 22% of cases. Thirty two percents of patients had at least one another cancer (most frequent: head and neck cancer [63/97], lung cancer [15/97]). Sixty percents of patients received chemotherapy.
Results: From the development cohort, the following putative PF have been retained by univariate analysis: associated cancer, previous chemotherapy, extra-mediastinal lymph nodes, dysphagia grade, weight loss, performance status and hemoglobin level. The Cox model has retained 2 PF, only: associated cancers (HR = 2.77 [1.39−5.54], p = 0.004) and grade 3−4 dysphagia (HR = 1.44 [1.08−2.14], p = 0.007). The median survival was 10.9, 6.2 and 1.8 months in patients with none (n = 77), 1 (n = 65) and 2 (n = 11/171) of these adverse PF, respectively (p = 0.025). The median survival of the patients with none, one and 2 adverse PF was 9 vs 13 months (non significant, ns), 5 vs 6 months (ns), and 1.3 vs 5 months (ns), whether or not the patients received chemotherapy, respectively. Patients with squamous cell carcinomas exhibited a similar pattern of survival than the whole cohort of MOEC, with or without chemotherapy.
Conclusion: We show here some evidence that chemotherapy has no or little impact on survival for MOEC, regardless of the PF we identified.

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Study to evaluate response to preoperative chemotherapy followed by postoperative chemoradiotherapy, expression of multidrug resistance gene and quality of life in locally-advanced gastric and gastroesophageal junction adenocarcinoma

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Background: We intended to assess the feasibility of combining neoadjuvant chemotherapy (NACT) with postoperative chemoradiation (POCRT) in locally advanced gastric/gastroesophageal junction adenocarcinoma (LAGC) along with multidrug resistance (MDR-1) gene expression & quality of life (QOL) assessment.
Materials and Methods: We enrolled 14 patients (pts) of LAGC (stage II-IV, age $\leqslant$70 years, KPS $\geqslant$70) in a single arm phase-II trial. After 2 cycles of NACT (cisplatin 80 mg/m^2 D1, capecitabine 2 g/m^2/day D1−14 q3 weeks), response was assessed by upper GI endoscopy & CECT abdomen. Pts with resectable tumors underwent radical total/subtotal gastrectomy with D2 lymphadenectomy & POCRT (45 Gy/25#/5 weeks, concomitant capecitabine 1.5 g/m^2/day). Inoperable pts received salvage chemoradiation (SCRT) or supportive care (BSC). Pre- & post-therapy (1 month) QOL was assessed by EORTC QLQ-C30 questionnaire (V3.0). MDR-1 expression was evaluated by flowcytometric assay of P-glycoprotein positivity.
Results: Median age was 50 years. Male to female ratio was 9:5. Tumor locations included GE junction/proximal stomach (4), distal stomach (8) & diffuse (2). Radiology showed N+ & T4 disease in 11 & 6 pts respectively. In 50%, tumors were initially unresectable. At a mean follow-up of 7.36 months, only 3 pts completed assigned treatment & all 3 had complete response (CR). Among others, locoregional progression, distant metastasis & noncompliance were noted in 28.6%, 21.4% & 28.6%, respectively. After NACT, response rate, disease control rate & symptomatic benefit were 28.6%, 57.2% & 78.6%, respectively. Only 1 of 7 unresectable pts became resectable post-NACT. Both NACT & POCRT were well tolerated (Gr 3/4 toxicity – NACT: hematologic-4, non-hematologic-6; POCRT: hematologic-1, non-hematologic-2). Pts with unresectable tumors received SCRT (1), palliative chemotherapy (1) or BSC (6). MDR-1 expression was monotonously low (mean 5.13%) & was not turned on after NACT (mean 3.2%). In the comparative analysis of pre-therapy & post-therapy QOL, Global health status (QL2) declined by 7.86%, social functioning declined by 28.8%, & financial difficulties increased by 33.69%.
Conclusions: NACT followed by POCRT is a novel & safe approach in LAGC. Still, only 21.42% pts completed assigned treatment & had CR, possibly owing to high noncompliance (28.6%) & adverse patient characteristics. More careful patient selection & longer follow-up will allow a more meaningful evaluation of this approach. MDR-1 pathway is probably not the major mechanism of chemoresistance in gastroesophageal adenocarcinoma in our patients.

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Prognostic significance of preoperative serum tumor markers in the patients with curatively resected advanced gastric cancers

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Background: We evaluated the prognostic significance of preoperative tumor markers, carcinoembryonic antigen (CEA), carbohydrate antigen 19−9 (CA19−9), and carbohydrate antigen 72−4 (CA72−4), in the patients with curatively resected advanced gastric cancers.
Methods: Six hundred and sixty seven patients who had been enrolled in a phase III trial of adjuvant chemotherapy (AMC0201) and preoperative serum tumor markers were available were eligible for this study. We compared the relapse free survival (RFS) and overall survival (OS) according to patient's pretreatment clinical characteristics and serum tumor markers using log rank test and Cox proportional hazard model.
Results: Of total 667 patients, 3 year RFS rate and OS rate were 67.4% and 75.0%, respectively. Postoperative pathologic stage was II in 353 (52.9%), IIIA in 202 (30.3%), IIIB in 61 (9.1%), and IV (M0) in 51 (7.6%). CEA, CA19−9, CA72−4 were elevated preoperatively in 64 of 665 patients (9.6%), 75 of 664 patients (11.3%), and 121 of 639 patients (18.9%), respectively. After median follow up of 3.2 years, 209 patients (31.3%) had recurrence, and 164 patients (24.6%) died.
In univariate analysis, location of tumor, type of surgery, Borrmann type, TNM stage, CEA elevation, and CA72−4 elevation were significant prognostic factors in RFS and OS. In multivariate analysis, CA72−4 was independent significant prognostic factor for RFS and OS as well as tumor location, Borrmann type, and stage.
Conclusion: Preoperative serum CEA and CA72−4 levels were independent prognostic factors as well as clinical characteristics of pathologic stage, tumor location and Borrmann type in patients with curatively resected AGC.

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Overexpression of tissue biomarkers associated with allelic alterations may have potential prognostic implications with different behavior in esophagus cancer

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Background and Aim: Expression of biomarkers and probable allelic alterations were studied in esophagus tissue samples from patients with esophageal carcinoma.
Methods: A total of 116 esophagus tissue samples were obtained from 25 patients with esophagus cancer. Histological studies revealed 23 samples were adenocarcinoma and 14 samples were epidermoid carcinoma while 79 samples were non-tumor. Expression of biomarkers was determined by enzyme immunoassay, and allelic alterations on chromosome 17 p were performed by polymerase chain reaction (PCR) using primers D17S513 and D17S514.
Results: The adenocarcinoma group exhibited an increase of matrix metalloproteinase (MMP)-1 ($P < 0.0001$) and sialyl Le (a) ($P < 0.001$) mean levels when compared with the non-tumor group. Adenocarcinoma samples from patients with more than three positive lymph nodes had lower levels of tissue-inhibitor metalloproteinase (TIMP)-1 than those with negative nodes ($P < 0.0005$). Positive allelic alteration was associated with high levels of MMP-1 expression ($P = 0.003$). Epidermoid carcinoma samples showed higher expression of MMP-1 ($P < 0.0001$) and TIMP-1 ($P < 0.02$) than non-tumor samples. Both epidermal growth factor receptor and sialyl Le (a) levels were overexpressed in tumors of patients with more than three positive lymph nodes ($P < 0.005$). Carcinoembryonic antigen levels were higher in tumors associated with allelic wild type group ($P = 0.0001$) and patients with negative lymph nodes ($P < 0.05$). Furthermore, variability in expression of biomarkers was observed according to sample location, and allelic alterations were also found both in tumor and in some non-tumor samples.
Conclusion: The data suggest that overexpression of tissue biomarkers associated with allelic alterations may have potential prognostic implications with different behavior in esophagus cancer.