

of 47 (34%) we noticed cytokeratines-positive cells in SLNs only, being the other nodes negative. Our skip metastases rate was 8.5% (4/47 patients).

Conclusion: We found that SLN reflects the status of all the other pericolic nodes. Thus, a more accurate analysis performed on SLN in colon cancer may help to identify an additional patient population who should be treated with adjuvant chemotherapy.

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POSTER

Efficacy of intraoperative cytological examination

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Background: The aim of the study was to assess the efficacy of intraoperative cytological examination.

Materials and methods: The efficacy of the method was analyzed on the basis of 2647 specimens obtained from 553 patients who were operated in 2002. Cytological specimens included biopsies, scrapes, imprints and body cavity fluids. We examined 609 biopsies of primary tumors and tumor-like masses from different sites, 44 liver biopsies, 756 lymph node scrapes, 330 surgical margins' scrapes (mainly breast, bronchi and esophagus), 232 scrapes and imprints from serosae, 213 scrapes and imprints from peritumoral tissues, 463 samples of pleural and peritoneal fluid. Cytological smears were stained using Papanicolaou's modified method (azur-eosin staining). The results of intraoperative cytological assessment were compared to the conventional histopathological examination.

Results: An overall accuracy of intraoperative cytological examination was 98.3%; false negative results were observed in 1%, false positive – 0.7%. The accuracy of intraoperative cytological examination for different cytological specimens was as follows: lymph node metastases – 99.2%, primary tumors – 95.9%, surgical margins – 99.7%, serosae – 97.8%, peritumoral tissues – 98.1%, hepatic lesions – 97.7%.

Conclusion: Intraoperative cytological examination is a highly accurate method of morphological diagnosis. Still some cytograms of malignant tumors were misinterpreted. In case of lymph nodes micrometastases and high-grade sinus-histiocytosis were the reasons of failure. In case of fluids and serosae non-specific mesothelial changes accounted for false results. In some instances it was difficult to differentiate tumor cells from non-specific inflammation.

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POSTER

Analysis of G/A SNP change at position 2494 in the E-cadherin gene in Italian patients with sporadic, diffuse gastric cancer

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Current investigations are studying new E-cadherin gene (CDH1) mutations that may be causative of diffuse gastric cancer susceptibility. Recently, a novel CDH1 germline variant with G/A nucleotide change at cDNA position 2494 has been found in Japanese patients with familial diffuse gastric cancer. The consequent amino acid variation (Val/Met) may alter the binding activity of B-catenin and the adhesive function of the E-cadherin protein. Data on the 2494 G/A nucleotide change in sporadic cases of diffuse gastric cancer and in patients of Western origin are lacking. We have investigated its frequency in Italian cases of sporadic, diffuse gastric cancer and healthy controls.

Peripheral blood samples were collected from consecutive patients with sporadic, diffuse gastric cancer and healthy controls who were natives of the District of Urbino, Region Marche, Central Italy. After DNA extraction, standard techniques for molecular analyses were used to investigate the 2494 G/A germline nucleotide change in CDH1 cDNA.

None of 48 patients and 48 controls showed the G/A 2494 nucleotide change. Assuming a binomial distribution of the mutation among individuals and according to zero mutations in 48 patients, the 95% upper bound for the underlying mutation frequency was 7.4%.

The novel CDH1 nucleotide change is uncommon in Italian patients with sporadic, diffuse gastric cancer. In this setting, further analyses in large population-based studies are not advisable.

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POSTER

Should gastrectomy be performed for metastatic stomach carcinoma?

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Background. The prognosis of patients with metastatic stomach carcinoma is extremely poor, and there exists controversy on the adequate surgical treatment in terms of safety and benefit.

Material and methods. We reviewed the outcome of 56 patients with metastatic gastric cancer in whom total or subtotal gastrectomy ± metastasectomy was performed. The sites of metastases were as the follows: peritoneum (18 patients), distant lymph nodes (16), liver (10), ovary (5), other sites and multiple sites (6). There were 33 males and 23 females; the mean age was 55 years. Tumor-related complications were registered in 40 patient, anemia (17) and pyloric stenosis (15) predominated. The primary tumor penetrated the serosa in 40 patients, involved two thirds or the whole stomach in 32 patients. Lymph nodes were positive in 33 patients. The study population was divided into two equal groups: 28 patients treated between 1975 and 1995, and 28 patients treated between 1996 and 2002.

Results. In the second period of the study, the portion of total gastrectomies increased from 39 to 57%, of extended (D2 or more) lymphadenectomy from 7 to 36%. At the same time the incidence of anastomotic leaks decreased from 14 to 7%, intraabdominal infection from 14 to 0%, pneumonia from 18 to 7%; overall number of patients with complications from 36 to 11%. Postoperative mortality was 25% in the former period and 3.5% in the latter. Complete resection of all metastatic sites was performed in 20 (36%) cases, partial resection in 9 (16%) cases. Median survival of the whole group (excluding postoperative deaths) was 8.2 months. Cumulative survival was as the follows: 6 months 76%, 1 year 34%, 2 years 8%. There were only 2 long-term survivors (43 and 115 months), both had distant lymph node metastasis.

Conclusions. Gastrectomy, including extended and combined resections, may be performed safely independently of the degree of metastatic extension. It should be performed to patients with metastatic gastric cancer to overcome or to prevent fatal tumor complications. In appropriate cases (P1, H1 etc.), complete metastasectomy may increase the effectiveness of adjuvant therapy and give a patient a chance for cure.

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POSTER

Outcome of patients receiving radiation with or without chemotherapy for squamous cell carcinoma of the esophagus

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Purpose: Several studies showed chemoradiotherapy for patients with esophageal cancer was superior radiotherapy alone. There were few studies whether these results were reproduced in practice. Primary objective of this study was to determine outcome of patients with esophageal cancer treated in our institution who received radiation therapy with or without chemotherapy.

Material & methods: From 1994 to 2001, 216 patients with squamous cell carcinoma of the esophagus without distant organ metastases were treated with curative intent using radiation therapy alone or combined chemotherapy at National Cancer Center Hospital, Tokyo. There were 186 males and 30 females. The age at diagnosis ranged from 40 to 89 years with a median of 64.5 years old. Forty-eight percent of patients (103 patients) had clinical stage (CS) 1 disease, 17% (37 patients) had CS 2 disease, and 35% (70 patients) had CS 3 disease. Fifty-one patients were treated with radiotherapy alone, and 165 patients were treated with radiotherapy and chemotherapy concurrently. Most of patients treated with chemotherapy were taken cisplatin and fluorouracil.

Results: At the time of the analysis, 128 patients were alive and 88 patients were dead. The median duration of follow-up for the patients alive was 27.0 months. A survival rate of all patients at 2 years was 63.6%. Patients, tumor and treatment-related factors were found to be significantly associated with survival on univariate analyses. At 2 years, patients with CS 1 disease had a 88.3% survival rate, compared with 56.3% for the patients with CS 2 and 33.7% for the patients with CS 3 ($p < 0.0001$). Patients who had chemotherapy with radiotherapy concurrently had a 68.5% 2-year survival rate, whereas those who did not had a 2-year survival rate of 44.8% ($p = 0.0038$). Two-year survival rate for patients who presented with a serum albumin level ≤ 3.7 g/dl was 70.7%, compared with 58.2% for patients with > 3.7 g/dl ($p = 0.0459$). Survival rate was lower for patients with

primary tumor in cervical esophagus versus those with in intrathoracic esophagus (46.2% vs. 64.9%, $p=0.0231$). Patient age, sex and hemoglobin level were not associated with survival. By multivariate analyses, stage and chemoradiotherapy were significant factors. Local control (including salvage cases by endoscopic mucosal resection) at 2 years was 61.9%. By multivariate analyses, stage and sex were significant factors. Patient age, hemoglobin level, serum albumin level, anatomical subsites and using chemotherapy were not associated with local control.

Conclusion: This study showed high survival rate and local control rate for patients with localized esophageal cancer treated by radiation therapy with or without chemotherapy. By multivariate analyses, stage and chemotherapy were significant factors on survival, and stage and sex were significant factors on local control.

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POSTER

Stent placement in malignant superior vena cava syndrome

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Background: Superior vena cava (SVC) syndrome is caused by SVC stenosis or occlusion, frequently as a consequence of a lung cancer or mediastinal tumor. SVC syndrome is characterized by unpleasant symptoms that usually lead to death. Treatment with radiation therapy and chemotherapy may produce an initial relief, whereas operations with bypass are associated with high mortality and morbidity. The purpose of our study is to show the efficiency of percutaneous stenting in the superior vena cava for relieving SVC syndrome secondary to malignant disease.

Material and methods: From January 1999 to March 2002, 17 patients with malignant SVC syndrome were evaluated at Metaxa Cancer Hospital. Their caval stenoses were confirmed by computed tomography and venography. There were 15 males and 2 females with an average age of 62 years (range from 47 to 79 years old). The SVC syndrome was caused by malignant disease in all patients: broncho-pulmonary cancers in 14 and lymphoma in 3. All patients underwent placement of a self-expandable (Wallstent) endovascular (vena cava) prosthesis. Results: All procedures were successfully carried out and there were no immediate complications. The average time for wallstent placement was 37 min. There was no sign of bleeding and the wallstent was well positioned on chest roentgenograms. All patients, without exception, noticed an immediate improvement, with relief of pressure and rapid resolution of headache. Cyanosis disappeared over the first hour and swelling resolved over the first 24h.

Conclusion: Percutaneous venous wallstent placement in the superior vena cava is a simple, safe and effective technique to relieve rapid SVC syndrome caused by malignancies.

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POSTER

Weekly gemcitabine with concurrent radiation for unresectable pancreatic cancer

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Background: Combined chemo-radiotherapy may improve local control, resection rate and long term survival in patients with locally advanced pancreatic cancer. Many oncologists consider concurrent 5 fluorouracil and radiotherapy as standard treatment for these patients.

Gemcitabine is an active agent in advanced pancreatic cancer resulting in clinical benefit in 30-50% of pts. and an objective response rate of 5-11%. Gemcitabine has known radiosensitizing properties. Various schedules have been tested with gemcitabine and radiotherapy.

Material and methods: From January 1999 to July 2002, 21 patients with locally advanced, unresectable pancreatic cancer were enrolled onto this study. Patients characteristics: there were 15 male and 6 female, median age 63 years (range 42 to 69), performance status ECOG 0-2, bilirubin plasma level < 2 mg/dl. A chemo-radiotherapy regimen consisting of weekly gemcitabine (200 mg/m²) with 45 Gy of external beam radiotherapy (1.8 Gy / fraction, 5 days / week) was delivered in five weeks. Patients were re-staged with chest radiographs and CT scans 4-6 weeks after treatment. Those with down-staging tumors and good performance status underwent pancreaticoduodenectomy.

Results: 17 patients completed chemo-radiotherapy schedule. 3 patients interrupted the treatment 2 because of grade 4 toxicity and 1 because of

progressive disease. Clinical benefit was found in 13 of the 17 patients (5 partial response and 8 stable disease). Progressive disease was found in the four remained patients. Six patients received surgery. Adverse effects, especially hematologic, were common but manageable. No chemoradiation-associated deaths were observed with this gemcitabine-based regimen. Grade 3 to 4 hematological toxicity (neutropenia and/or thrombocytopenia) occurred in 7 and 2 patients respectively. Grade 3 gastrointestinal toxicity (nausea, vomiting and diarrhea) occurred in 3 patients. There was no grade 4 gastrointestinal toxicity. The median time to progression was 8 month and the median survival was 14 month.

Conclusions: This schedule of Gemcitabine and radiation therapy is well tolerated, and has shown to provide prolonged clinical benefit response and disease stabilization in patients with localized, unresectable pancreatic carcinoma. The potential of this regimen to downstage a subset of previously unresectable patients should be further investigated using modern techniques of radiation delivery like three dimensional conformal radiotherapy.

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POSTER

Fortnightly intravenous irinotecan plus oral capecitabine as treatment for gastroesophageal cancer – a phase 1 and 2 study.

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We investigated a combination of intravenous irinotecan and oral capecitabine (IriCap) in patients (pts) with locally advanced or metastatic gastroesophageal adenocarcinoma. The design employed cohort dose-escalation during phase I to establish maximum tolerated dose (MTD), then a 31-patient phase II study at MTD to estimate efficacy. In phase I, cohorts of at least 4 pts received each of the following dose levels: *Level 1:* irinotecan 150 mg/m² i.v. infusion, d1; capecitabine 850 mg/m² p.o. 12-hourly d1-9, 14-day cycle. *Level 2:* as level 1 but capecitabine 1000 mg/m². *Level 3:* as level 2 but irinotecan 180 mg/m². *Level 4:* as level 3 but capecitabine 1250 mg/m². For pts entered at levels 1 and 2 only, intra-cohort dose escalation after 3 cycles was allowed. Pts were monitored for toxicity, and assessed for response after 6 cycles.

21 pts were entered in Phase I. Dose-limiting toxicity occurred in 1 of 5 pts started at dose level 1 (Gr 3 lethargy); 1 of 8 pts started at or escalated to dose level 2 (Gr 3 mucositis); 0 of 6 pts treated at dose level 3; and 6 of 7 pts treated at dose level 4 (1 Gr 3 vomiting, 3 Gr 3 lethargy, 1 Gr 3 diarrhoea and 1 Gr 4 diarrhoea). Accordingly, level 3 was declared MTD, and used during Phase II.

31 chemo-naïve pts were entered in Phase II. A total of 165 cycles were delivered, 61% of pts receiving at least 6 (mean = 5.3). Grade 3 toxicities were lethargy (6 pts), diarrhoea (5 pts), nausea (3 pts) and anorexia (3 pts). During the first 6 cycles 74% of treatment cycles were given at full dose, but 15 pts underwent dose reduction (of both drugs) for toxicity. 3 pts stopped treatment before cycle 6 because of toxicity and 8 because of early PD. There were no treatment-related deaths. 28 pts were assessable for response (RECIST): PR = 9 (32%), SD = 9 (32%) and PD = 10 (36%). Of the 9 pts with SD, 4 had evidence of treatment activity (3 minor response on CT, 1 tumour marker response, all with symptomatic improvement).

This fortnightly IriCap schedule is active in gastroesophageal adenocarcinoma with a response rate, in this unrandomised trial, similar to standard chemotherapy schedules. In the Phase II study at dose level 3 (irinotecan 180 mg/m² d1; capecitabine 1000 mg/m² 12 hourly d1-9, q14d), a relatively high proportion of pts (16/31, 52%) required dose reduction or stoppage for toxicity during the first 6 cycles; further modification of the schedule is therefore required to reduce the toxicity profile for further study.

Supported by an unconditional grant from Aventis Pharma Ltd, UK.