Results: Median age of the patients included in the study was 59.9 years (range, 40-80). Mean carcinomatous and sarcomatous component were 55.2% (range, 10-95%) and 44.7% (range, 5-90%), respectively.

Primary tumor sites were ovary and endometrium in 59.9% and 47.7% of patients, respectively. There were 5.8% of patients in stage IIB, 11.7% in stage IIIB, 47.1% in stage IIIC and 23.5% in stage IV. 94.1% of patients had metastatic disease. The most common metastatic sites were omentum, ovaries, colon, appendix and tuba. There were also two patients with liver metastasis. 10 out of 17 patients (58.8%) were treated with a combination chemotherapy regimen of cisplatin-ifosfamide (PI) and seven patients (40.2%) were treated with paclitaxel-carboplatin (PC) protocol. One patient whose tumor contains 80% carcinomas and 20% sarcomas had a consolidation radiotherapy to the pelvic region after chemotherapy. Median number of chemotherapy cycles was 6(range: 3-9). 18.8% of patients had progressive disease despite chemotherapy. The remaining 13 patients (81.2%) responded to chemotherapy; there were 7 patients with CR and 6 patients with PR and stable disease. Response rates of patients treated with PC (100%) were remarkably higher than the response rates of patients treated with PI (80%). Patients with predominating carcinomatous component had a higher response rate(88.8%) than patients with predominating sarcomatous component(60%).

Conclusion: MMMT are highly chemoresponsive tumors, irrespective of primary site. One of the best predictors to response is the histologic pattern. Predominating histopathologic feature (carcinoma or sarcoma) should be taken into consideration in predicting the response and planning the chemotherapy regimen.

189 POSTER

Evaluation of human papilloma virus infection in cervical cancer and P53 gene mutations.

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Cancer of uterine cervix is one of the most prevalent cancers in women, after breast cancer. Infection with high risk Human Papilloma Virus (HPV) and disfunctioning of P53 tumor suppressor gene due to molecular lesions are thought to be the main carcinogenesis factors in cervical cancer. To study the prevalence of HPV infection and status of P53 tumor suppressor gene, 50 paraffin embedded tissue samples with stage specific pathological diagnosis of cervical cancer collected from the university hospitals. DNA was extracted from tissue sections and PCR amplified using general, HPV16, and 18 type specific primers. To detect mutations in P53 gene, after PCR amplification of the desired exons the PCR products were subjected to single strand conformation polymorphism (SSCP) analysis. Thirty-seven samples were positive for HPV infection. Out of these 37 samples, 23 were positive for HPV16 and 4 samples for HPV18. Results of SSCP analysis of P53 gene demonstrated polymorphism in 4 samples, among which 3 were from HPV positive and 1 from HPV negative samples. Our results clearly demonstrate the importance of HPV infection in cervical cancer. HPV16 showed higher prevalence than HPV18 which indicates the important rol of HPV16 in cervical neoplastic transformation. Also there might be a relationship between P53 mutations and HPV infection in this cancer among the patients under study.

190 POSTER

E-cadherin and beta catenin immunoexpression in primary ovarian carcinomas: an association with clinicopathological features.

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Backround Epithelial cadherin is an cell-cell adhesion molecule that forms a complex with alpha, beta and gamma catenin proteins. Reduced expression of E-cadherin and catenins has been associated with low histological differentiation, invasiveness and metastatic disease in human carcinomas.

Aim: Evaluate E-cadherin and beta catenin immunoexpression pattern (reduced *versus* preserved phenotype) in ovarian carcinomas and its relation with clinicopathological features

Materials and Methods Immunohistochemical analysis of E-cadherin and beta catenin in 104 carcinomas.

Results The immunoexpression pattern of E-cadherin correlated with histological subtype ($p<0.01$), peritoneal implants ($p=0.006$), and residual tumour ($p=0.04$). The preserved phenotype of E-cadherin in 37/104 carcinomas associated with mucinous carcinomas, absence of peritoneal implants and residual tumour. Whereas, the reduced phenotype of E-cadherin in 67/104 carcinomas associated with advanced stage tumours, serous carcinomas, presence of peritoneal implants and residual tumour >2cm after cytoreductive surgery.

The immunoexpression pattern of beta catenin correlated with histological subtype ($p<0.01$), tumour differentiation ($p=0.02$), and peritoneal implants ($p=0.04$). The preserved phenotype of beta catenin in 27/104 carcinomas associated with well/moderately differentiated tumours, serous, mucinous and endometrioid histological subtypes, absence of peritoneal implants and residual tumour. Whereas, the reduced phenotype of beta catenin in 77/104 carcinomas associated with advanced stage tumours, poorly differentiated serous and clear cell carcinomas, presence of peritoneal implants and residual tumour.

The immunoexpression pattern of E-cadherin correlated with that of beta catenin ($p<0.001$). The simultaneous immunoexpression patterns of E-cadherin and beta catenin significantly associated with peritoneal implants ($p<0.001$), and histological subtypes ($p=0.001$).

Conclusion The immunohistochemical profile of E-cadherin and beta catenin was shown to be of biological relevance and may provide new insight into the biology of ovarian carcinogenesis. Since, the reduced phenotype of these molecules was shown to associate with aggressive biological behaviour, increased invasiveness and peritoneal implants.

Other gastro-intestinal tumours

191 POSTER

Phase II trial of gemcitabine and capecitabine (GemCap) in patients with advanced biliary cancer.

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Background: Advanced biliary cancer is an aggressive cancer with a median survival time of under 6 months. Chemotherapy has shown minimal activity with little impact on overall survival. Recent phase II trials suggest that newer agents such as gemcitabine or capecitabine have activity (19-35% RR) in this disease. Preclinical data suggests synergy between gemcitabine and capecitabine. We conducted a phase II trial to study the efficacy and toxicity of both drugs in combination in patients with advanced or metastatic biliary cancer.

Methods: Patients with unresectable cholangiocarcinoma or gallbladder cancer were enrolled from July 2001 onward. Eligible patients had histologically or cytologically confirmed adenocarcinoma, no prior systemic therapy, ECOG PS $\leq$ 2, serum total bilirubin up to 3 x normal and measurable disease. Treatment consisted of gemcitabine 1000 mg/m ^{2} IV day 1, 8 concurrent with capecitabine 650 mg/m ^{2} PO BID day 1 to 14, on a 3 week cycle (Hermann et al, Proc. ASCO, 2000). Tumor response was assessed by RECIST criteria.

Results: Of the 25 patients enrolled to date 12 (48%) had cholangiocarcinoma and 13 (52%) had gallbladder cancer. Median age was 62 (range 45-81). A total of 128 cycles of chemotherapy was administered, for an average of 5.4 cycles per patient (range 1-15). At median follow-up of 4.2 months, 25 patients are evaluable for toxicity and 21 for response. There are 6 partial responses (29%), plus an additional 9 patients with stable disease > 3 cycles (43%). Median time to disease progression is 6.3 months. Overall survival is 9.6 months. No grade 4 toxicity was seen (see table below). Grade 3 neutropenia (no febrile neutropenia) and manageable hand-foot syndrome were most common.

Common Toxicity	Percentage of patients (worse toxicity, n = 25)	
	NCI grade 2	NCI grade 3
Neutropenia	4	20
Thrombocytopenia	0	12
Hand-Foot syndrome	12	16
Fatigue	16	4
GI	12	0

Conclusions: GemCap is an active and extremely well tolerated chemotherapy regimen in patients with advanced biliary cancer. GemCap has an objective response rate comparable to or better than most other phase II data, but also demonstrates durable disease stabilization, encouraging median survival and mild toxicity. Anticipating that this regimen will have

clear patient benefit, a phase III study is planned. Patient accrual is ongoing and updated results will be presented. Sponsored in part by Roche Canada.

192 POSTER

Gastrectomy with small intestine reservoir formation

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Introduction. Modern technologies of the gastric cancer surgery allow to increase the duration of patients' life. However, negative consequences like reflux-esophagitis and digestive disorders because of reservoir function absence can appear in remote postoperative period. New method of esophago-intestinal anastomosis was elaborated as objective to improve functional results of gastrectomy.

Materials and methods. Gastrectomy was carried out in 104 patients with cancer of the stomach (94 cases) and cancer of gastric stump (10 cases). The cancer stage was T 3-4 N 1-2 M 0, that's why mobilization of the stomach with lymphodissection at the extent of D 2 was performed. The stomach with paraesophageal fat was extirpated, in 27 patients it was made in combination with affected organs. In 7 cases we used thoracoabdominal access. The initial part of jejunum was leaded and fixed around esophagus like a sleeve. Perimesenterial enteroplication of both loops beginning from the esophagus to the extent of 15-20 sm was performed. In the part of enteroplication intestinal walls were dissected, then posterior wall of reservoir was formed with continuation to the left and right esophageal semicircle. The anterior wall of dissected jejunal loops was sutured and esophagus was immersed into reservoir. We made the second line of suture over immersed esophagus and on anterior wall of reservoir. Then we formed intestinal anastomosis with the covering of afferent loop, in cases of gastric stump extirpation the afferent loop was connected as Rue-anastomosis.

Results. Postoperative complications had 8 patients (7,6%). Incompetence of esophago-intestinal anastomosis had 2 patients. Seven patients died (6,7%) due to: incompetence of esophago-intestinal anastomosis 1, incompetence of intestinal anastomosis 1, commissural intestinal impassability 1, bile peritonitis after hepar resection 1, thrombosis of mesenterial vessels 1, acute myocardial infarction 2 cases. After 6-24 months of postoperative period there was not reflux-esophagitis, formed reservoir functioned good and provided portion evacuation. Three patients had transient dysphagy, one of them underwent with dilatation of esophago-intestinal anastomosis.

Conclusion. Suggested method of esophago-intestinal anastomosis formation has high level of reliability, prevent from development of reflux-esophagitis and compensate reservoir function after gastrectomy.

193 POSTER

Development of early gastric cancer 4 years after complete remission of Helicobacter pylori-associated gastric low-grade B-cell MALT lymphoma

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Aim: To report on 2 patients with Helicobacter pylori associated gastric MALT lymphoma who developed early gastric cancer 4 years after complete lymphoma remission following cure of helicobacter pylori infection.

Patients and Methods: Two patients (one male 74 years; one female, 62 years) with Helicobacter pylori-associated low-grade MALT lymphoma. Both patients achieved complete lymphoma remission after being cured of the infection. Surveillance endoscopies were performed twice yearly. The patients were helicobacter pylori negative during the whole follow up time.

Results: Four years after cure the infection and complete lymphoma remission, the patients presented with early gastric adenocarcinoma of the mucosa type (Z 4mm), type IIa and type IIc, resp., which both were completely removed by endoscopic mucosal resection. In one patient the gastric cancer was diagnosed at the same localization as the previous MALT lymphoma, in the other patient it was detected at a different site of the stomach, opposite from the previous MALT lymphoma.

Conclusion: These findings strengthen the importance of regular long-term follow up endoscopies in patients with complete remission of gastric MALT lymphoma after cure of Helicobacter pylori infection.

194 POSTER

In-DOTATOC: An useful diagnostic method for pancreatic tumor

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Purpose: Somatostatin receptors have been identified in different kinds of tumors. These observations have served as the DOTA-Tyr3-octreotide (DOTATOC), a somatostatin analogue, basis for the clinical use of radio labelled with indium-111 (^{111}In) for diagnostic purposes.

Materials and Methods: Twenty rats will be divided into four groups. They will be sacrified at 0.5, 4, 24, 48hrs (5 in each group) after injection of approximately 3.7 MBq of ^{111}In-DOTATOC. Samples of various organs will be obtained and counted to calculate the tissue concentration and estimated radiation dose. Different dose of ^{111}In-DOTATOC will be added to the cell line to evaluate radiation effect of ^{111}In-DOTATOC in vitro. In addition, toxicity of ^{111}In and DOTATOC will also be evaluated by the Development Center of Biotechnology.

Results: After injection In-DOTATOC, the uptake ratio is 1.7199, 1.4803, 1.3645, 1.3706 on four times point. As time goes by, the tumor uptake ratio still in high. And we could see clearly AR42J tumor images by gamma-detected scientigrapgy. Easy to diagnosis somatostatin positive tumor.

Conclusion: DOTATOC, labelled with ^{111}In, is not only a possible new diagnostic agent, but could give its superior biokinetics and especially kidney-to-tumour uptake ratio. A new therapeutic alternative for DOTATOC when labeled with a *-emitter like ^{90}Y for diagnostic and radionuclide therapy applications.

195 POSTER

Photodynamic therapy (PDT) of esophageal cancer: 11-years clinical experience.

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In the Moscow P.A. Hertzen Research Oncology Institute PDT has been treating esophageal cancer patients since 1992. In our practice Photogem (hematoporphyrine derivative), Photosens (sulfonated aluminium phtalocyanine),Radachlorin (natural chlorophill-α derivative), Alasens (5-aminolaevulinic acid) are used as photosensitisers. Up to this time, all of 84 patients with esophageal cancer in I-IV stages have been treated with PDT (male 56, female 28, average age – 68,3 years) .A Ist stage of esophageal cancer (T1N0M0) was diagnosed in 31 patients, a IInd (T2N0M0)- in 20, a IIId and a IVth (T3-4N1M0-1)- in 33. Among the Ist group of patients the tumours were from 1 cm (in 11 patients) to 2 cm (in 20 patients) in size with a penetration into the mucous (5) or submucous (26) layer of the esophageal wall. In 25 cases it was squamous-cell carcinoma and among 6 patients it was adenocarcinoma in Barrett's esophagus. Among the IInd group were patients with squamous-cell carcinoma, in whom at the time of their complete examination (in which included endoscopical, endosonographical and morphological testing and CT) it was suspected that the tumour had invaded the in muscle layer to a limited degree, and the size of the tumour was less than 2 cm in 11 patients, from 2 cm to 3.5 cm – in 9 patients. The IIId group consisted of the patients with advanced stenotic esophageal cancer (3-8 cm long and II-III degree of dysphagia). Complete remission resulted in 22 of 31 patients in the Ist group (71%) and in 9 of 20 patients in the IInd group (45%).The follow up period was up to 9 year. A recurrence of the cancer was diagnosed in 9 patients of the Ist group and in 4 of the IInd group. The goal of PDT in patients of the IIId group was restoring esophageal lumen, reducing the size of the tumour and improving the quality of life. Lumen restoration was effective in 94,6% of the patients. In 25 patients the final stage of recanalization was placement of esophageal stents produced by the company "Wilson-COOK Medical inc" (USA) and "Rusch GmbH" (Germany) followed by multiple PDT courses through the stent. The average duration of life for those in the IIId group was 6 monthes. Based on this experience PDT is considered to be usefull in treating inoperable patients with esophageal cancer both with curative and palliative effects.