of patient distress, and these discrepancies are useful for identification of patients with a low HRQOL.

504 POSTER DISCUSSION

Advanced esophageal cancer patients treated with hydroxyurea, leucovorin, 5-fluorouracil and cisplatin (HLFP regimen)

J. Taieb[1], P. Artru[1], C. Louvet[1], M. Mabro[1], E. Carola[2], E. Lucchi[1], M. Krulik[1], A. de Gramont[1]. [1]*Saint-Antoine Hospital, Internal Medicine-Oncology, Paris;* [2]*Senlis Hospital, Internal Medicine, Senlis, France*

Aim: Treatment with a multimodulation of 5-fluorouracil (5-FU), with leucovorin and hydroxyurea, plus cisplatin has been shown to be active in advanced gastric carcinomas. We studied response rate, survival and tolerance in patients with nonresectable, locally advanced or metastatic esophageal carcinoma treated with this combination.

Patients and Methods: Eighty one patients (pts) were prospectively enrolled in the study: 72 men, 9 women; mean age 60.5 years; metastatic disease in 44 pts, locally advanced in 37 pts; baseline performance status (OMS) 0 (29 pts), 1 (35 pts), 2 (17 pts). Sixty nine pts had squamous cell carcinoma and 12 had adenocarcinoma. Treatment consisted of oral administration of hydroxyurea 1 g/m^2 per square meter on days −1, 1 and 2, 2 hour infusion of leucovorin 200 mg/m^2, 5-FU bolus 400 mg/m^2 followed by 5-FU 22-hour infusion 600 mg/m^2 on 2 consecutive days, every two weeks; and cisplatin 80 mg/m^2 on day 3 every two cycles.

Results: Response rate in 79 pts with mesurable disease was 54%. A weight increase was observed in 46%, and dysphagia disappeared in 60% of our pts. Surgery (7 pts) or radiotherapy (16) was performed in 62% (27/33) of nonmetastatic pts. Median progression free survival and overall survival were 9 and 13 months, respectively; there was no significant difference for these data between adeno- and squamous cell carcinomas. Grade 3/4 toxicity occurred in 34.5% of the patients, with grade 3–4 neutropenia in 19% and grade 3 thrombocytopenia, vomiting or diarrhea in 5% of the patients.

Conclusion: The HLFP regimen is an active and well tolerated chemotherapy for advanced or metastatic esophageal cancer.

505 POSTER DISCUSSION

Tobacco, alcohol and the risk of stomach cancer in Canada

J. Hu, Y. Mao, A.-M. Ugnat. *Cancer Bureau, LCDC, Health Canada, Ottawa, K1A 0L2, Canada*

Purpose: To examine the influence of tobacco and alcohol on the risk of stomach cancer.

Methods: Mailed questionnaires were used to obtain data on 1173 newly diagnosed histologically confirmed stomach cases and 4778 population controls between 1994 and 1997 in eight provinces of Canada. Data were collected on socioeconomic status, smoking, alcohol use and diet. Odds ratios (OR) and 95% confidence intervals (CI) were derived by logistic regression.

Results: Compared with never smokers, the risk of stomach cancer increased with increasing cigarettes per day. The adjusted ORs were 1.6 (CI = 1.2–2.0) and 1.36 (CI = 1.0–1.9) for >=20 cigarettes per day among males and females, respectively. The risk also increased with total smoking years and decreased with number of years since quitting. Liquor use was associated with stomach cancer in males, but not in females.

Conclusions: This study adds further support to the role of tobacco and liquor use in the development of stomach cancer.

506 POSTER DISCUSSION

5FU as protracted continuous IV infusion (5FUpiv) can be added to full dose taxotere-cisplatin (TC) in advanced gastric carcinoma (AGC)

A.D. Roth[1], R. Maibach[1], N. Fazio[2], O. Pagani[1], R. Morant[1], R. Stupp[1], F. De Braud[2], C. Sessa[1], M.M. Borner[1], R. Herrmann[1], A. Goldhirsch[1,2]. *Swiss Group for Clinical Cancer Research (SAKK), 3008 Bern, Switzerland;* [2]*European Institute of Oncology (EIO), Milan, Italy*

Based on the reported efficacies of TC (ASCO Proc. 17, 283a, 1998) and of 5FUpiv with cisplatin and epirubicin (J clin Oncol 15, 261, 1997) in AGC, we conducted a phase I–II trial investigating the tolerability and, as secondary endpoint, the activity of 5FUpiv added to TC (TCF) in AGC. Pts with AGC, without prior palliative chemotherapy, with evaluable disease, PS ≤ 1, normal blood counts and hepatic and renal functions received up to 8 cycles of TCF q3w at the following dose levels (DL):

DL	Pts	Cisplatin	Taxotere	5FUpiv 2 wks/3
1	12	60 mg/m^2	70 mg/m^2	200 mg/m^2/d.
2	6	60 mg/m^2	85 mg/m^2	200 mg/m^2/d.
3	6	75 mg/m^2	85 mg/m^2	200 mg/m^2/d.
4	3	75 mg/m^2	85 mg/m^2	225 mg/m^2/d.
5	6	75 mg/m^2	85 mg/m^2	250 mg/m^2/d.
6	3	75 mg/m^2	85 mg/m^2	275 mg/m^2/d.
7	3	75 mg/m^2	85 mg/m^2	300 mg/m^2/d.
8	4	75 mg/m^2	85 mg/m^2	350 mg/m^2/d.

To date, 188 cycles of treatment have been given to 43 pts with a median of 4 cycles/pt. 82% of the cycles could be given on time. Two dose limiting toxicities (tox) – defined as grade (gd) 4 neutropenia with fever and/or gd 3 tox of any other kind apart from alopecia in cycle 1 – consisting in gd 3 diarrhea + mucositis and in febrile neutropenia in 2 pts occurred in DL8. We conclude that DL7 is the MTD and recommended dose, and that TCF, with a preliminary response rate of 50%, is active in AGC.

507 POSTER DISCUSSION

Eight-hour infusion versus bolus injection of doxorubicin in EAP regimen in patients with advanced gastric cancer (AGC): A prospective randomised trial

I. Popov, S. Jelić, D. Radosavljević, Z. Nikolić-Tomašević. *Institut za onkologiju i radiologiju Srbije, Belgrade, Yugoslavia*

Purpose: Doxorubicin is carrier of myelotoxicity in EAP (doxorubicin 40 mg/m^2, etoposide 360 mg/m^2, cisplatin 80 mg/m^2) regimen. The aim of this study was to compare a 8-hour infusion doxorubicin (arm A) and i.v. doxorubicin injection (arm B) in EAP regimen with respect to toxicity esspecially doxorubicin-related, objective response, time to progression (TTP) and survival in pts. with AGC.

Methods: 120 chemotherapy-naive pts. with measurable AGC were randomised between September 1994 and August 1998. 58 pts. in arm A and 50 pts. in arm B were considered as evaluable. Arms were balanced in relation to age, sex distribution, previous therapy, histological grade and performance status. 180 cycles were applied in arm A (median 2) and 201 in arm B (median 4).

Results: No difference was detected (p = 0.12) in the response rate achieved: arm A 21% (CR 3/58; PR 9/58; 95%CI: 12.5–23.7) and B 34% (CR 3/50; PR 14/50; 95%CI: 22.4–47.8). There was significant difference in PD (p = 0.005) between arm A (50%) and arm B (24%). TTP (p = 0.01) and survival (p = 0.02) analyses detected an advantage for arm B vs. arm A. WHO grades 3–4 toxicity were (arms A%/B%): anemia 8/10, leucopenia 24/26, thrombocytopenia 6/16 (significance p = 0.05), nausea/vomiting 5/8, diarrhea 6/2, mucositis 8/5. Four treatment related death was occurred, 2 in each arm.

Conclusion: Bolus injection of doxorubicin is superior to 8-hour doxorubicin infusion in EAP regimen, in terms of survival, TTP and PD rate without being significantly more toxic.

508 POSTER DISCUSSION

Randomized trial of preoperative (PRT) and intraoperative (IORT) radiotherapy versus surgery alone in resectable gastric cancer

V. Skoropad, B. Berdov. *Medical Radiological Research Center of Russian Academy of Medical Sciences, 249020 Obninsk, Russian Federation*

Purpose: To evaluate the outcome of adjuvant PRT and IORT in resectable gastric cancer a prospectively randomized clinical trial was performed from 1993 to 1998.

Methods: Eighty five patients underwent curative operation were included in the study. Forty three patients in the experimental group were treated with PRT (27 Gy/11 days), gastrectomy and IORT (20 Gy using 8–12 MeV electrons); 42 patients in the control group- with surgery alone.

Results: Experimental treatment regime showed good acute and late tolerance. The median follow-up time is 27 months. Loco-regional recurrence was diagnosed in 2 (5%) patients in the experimental and in 7 (16%) – in the control group, distant metastases – in 9 (21%) patients in each group. Recurrence-free interval was significantly longer in the experimental group comparing with the control one: 22.4 (5–50) months and 9.9 (4–24) months respectively. Overall survival was slightly better in the experimental group: 77% (33/43 patients) and 66% (28/42).

Conclusion: The proposed aggressive treatment program of gastric cancer is feasible, well tolerated and is able to induce a high loco-regional tumor control rate.

509 POSTER

Clinical study on intraperitoneal hyperthermic perfusion chemotherapy for patients with gastric cancer

X.F. Cao[1], W.M. Wu[2], H.Y. Qiu[1], B.C. Wu[1], M.H. Cai[1], W.Z. Za[3]. [1]*Yan Cheng Cancer Hospital, Jiang Su Province;* [2]*The Affiliated Hospital of Nei Meng Gu Medical College,* [3]*The first People's Hospital of Yan Cheng, Jiang Su Province, China*

Purpose: The prognosis of patients with gastric cancer treated by only surgery are mostly still bad in China. We used intraperitoneal hyperthermic perfusion chemotherapy to hope to increase resection rate and survival rate, and to prevent the side effects of systemic chemotherapy.

Methods: 420 cases with gastric cancer were divided into five groups. Both Group A and Group B have 60 cases. Whereas Group A received neo-adjuvant intraperitoneal hyperthermic perfusion chemotherapy, Group B did not. Group C, Group D and Group E have 100 cases for each group. Group C received intraperitoneal hyperthermic perfusion chemotherapy; Group D accepted adjuvant chemotherapy; Group E did not received chemotherapy.

Results: The resection rate for Group A was 98.33% (59/60), whereas the resection rate for Group B was 86.33% (53/60) ($p < 0.05$). The rate of side effects of chemotherapy for Group C was 8% (II°), 2% (III°), 1% (IV°), which were lower than 30% (II°), 12% (III°), 6% (IV°) for group D respectively ($p < 0.05$). The 1 year and 3 year survival rates for Group A and Group C were higher than respective ones for Group B and Group C/D ($p < 0.05$).

Conclusion: Intraperitoneal hyperthermic perfusion chemotherapy may increase the resection rate and survival rate and prevent the side effects of chemotherapy. The exact value of intraperitoneal hyperthermic perfusion chemotherapy are worth further randomized study.

510 POSTER

Evaluation for multiple cancer in cases of endoscopic mucosal resection for early gastric carcinoma

T. Suzuki, T. Nakamura, A. Matsu-ura, K. Yamao, K. Ohashi. *Dept. of Gastroenterology, Aichi Cancer Center Hospital, Nagoya, Japan*

Purpose: Endoscopic mucoal resection (EMR) for early gastric carcinoma is a safe and minimally invasive treatment. Meanwhile, there is a need for the continued endoscopic surveillance in search of metachronous multiple lesion. This is because the patient treated with EMR has a whole stomach, the mucosa of which is considered to have a potential for carcinogenesis. In this study, we investigated the clinicopathological features of multiple gastric cancers in the patients who were treated by EMR.

Methods: The indications for EMR were those approved by the Japanese Endoscopy Society. The resection method used was double-channel technique with saline injection into the submucosa. A total of 115 patients (84 men, 31 women, mean age 66.6 years) with 127 lesions underwent EMR during the last 7 years. They were endoscopically followed every 3 months in the first year, and annually thereafter.

Results: Multiple gastric cancer was observed in 14 patients (12.2%) with 31 lesions. Double cancer was found in 11 patients, of which 5 were synchronous and 6 were metachronous. Gross appearances of the lesions were elevated-type (E)-E in 5, depressed-type (D)-D in 5, and E-D in one. In 7 of 11 cases, lesions occupied the same one-third of the stomach: middle one-third in 4 and lower one-third in 3. Triple cancer was found in 3 patients. Of these, all lesions were metachronous in 2 cases, whereas 2 lesions were synchronous in the remaining case. For these patients, gross appearance was D-D-D in 2 and E-D-D in one.

Conclusions: The incidence of multiple cancer in the EMR cases was proved to be high. The multiple lesions were liable to appear in the same macroscopic form and location. It is advisable to be aware of the possibility of finding the multiple lesions both before and after the EMR.

511 POSTER

Expression of thymidylate synthase and its prognostic value in gastric carcinoma with adjuvant 5-fluorouracil containing chemotherapy

H.Y. Lim[1], J.H. Choi[1], H.S. Kim[1], D.K. Nam[1], H.C. Kim[1], H.J. Joo[2]. [1]*Ajou University School of Medicine, Hematology & Oncology, Suwon;* [2]*Ajou University School of Medicine, Pathology, Suwon, South Korea*

Purpose: The antimetabolite 5-fluorouracil (5-FU) is one of the most common chemotherapeutic agents for gastric carcinoma. Thymidylate synthase (TS) is the target enzyme for 5-FU and intratumoral expression of TS may predict an inverse relationship to response and survival for patients who receive 5-FU containing chemotherapy. We investigate the expression of TS and its prognostic value in gastric cancer patients with adjuvant 5-FU containing chemotherapy after curative resection.

Methods: We obtained tissue specimens from 104 patients of surgically resected stage II and III gastric adenocarcinoma. All patients received adjuvant chemotherapy containing 5-FU after curative resection and extensive lymph node dissection. We performed immunohistochemical studying for TS with anti-TS antibody in gastric carcinoma.

Results: The positive rate of TS expression was 76.9% in 104 gastric cancers. The group with high and low TS expression consisted of 51.0% and 49.0%, respectively. The differences in recurrence and death rate between TS positive group and negative group were not significant (DFS 61.3% vs. 58.3% $p = 0.732$, OS 63.8% vs. 58.3% $p = 0.625$, respectively).

Conclusion: Our results suggest that TS expression alone could not predict the recurrence and survival in gastric carcinoma with adjuvant 5-FU containing chemotherapy after curative resection.

512 POSTER

Effects of high dose-rate intraluminal brachytherapy (HDR-ILBRT) for the patients with esophageal squamous cell carcinoma (SCC)

M. Iwasa[1], Y. Iwasa[1], Y. Ohmori[1], M. Kume[1], S. Ogoshi[1], Y. Ogawa[2], S. Yoshida[2]. [1]*Department of Surgery II;* [2]*Radiology Kochi Medical School, Nankoku, Kochi, Japan*

Background: The effectiveness of the multimodal treatment for the patients with esophageal SCC with HDR-ILBRT by 60 Co as a component of treatment was evaluated clinically.

Patients and Treatment Methods: 167 patients with esophageal cancer were divided into 4 treatment groups with or without operation and HDR-ILBRT: Group A: 71 patients were performed radical operation, external irradiation and HDR-ILBRT; Group B: 30 patients underwent operation and external irradiation only; Group C: 28 patients with external irradiation and HDR-ILBRT; Group D: 38 patients with external irradiation alone and no other modality.

Results: 5-year survival rate of Group A and B was 63% and 20%, respectively ($p < 0.001$). Mean Survival time and 5-year survival rate of Group C (15.3 ± 1.5 months and 20%) were significantly improved compared to Group D ($p < 0.001$). There was no 5-year survival in the patients without brachytherapy.

Conclusion: These results strongly suggest the use of HDR-ILBRT as a component of multimodal treatment in patients with esophageal cancer is a reasonable approach and HDR-ILBRT significantly improves the effects of external beam irradiation therapy.

513 POSTER

Effect of T and N stages on outcome of chemoradiation for carcinoma of anus

S. Ngan[1], J. Smith[2], M. Chao[1], D. Lim-Joon[1]. [1]*Peter MacCallum Cancer Institute, Radiation Oncology, Melbourne;* [2]*Peter MacCallum Cancer Institute, Statistic Centre, Melbourne, Australia*

Purpose: Chemoradiation has become the standard of care in management of anal cancer. Pathologic confirmation of the clinical stage is usually not available. This study was designed to investigate the effect of T and N stages in patients with carcinoma of anus treated with modern combined radiotherapy and chemotherapy.

Methods: Patients with localized squamous carcinoma of anus treated with curative intent with chemoradiation between 1 January 1982 and 31 December 1996 were identified from the anal cancer database at Peter MacCallum Cancer Institute. The standard protocol during this period consisted of radiotherapy of 54 Gy in 30 fractions with chemotherapy 5-FU