Methods: Patients (pts) were randomized to receive FLO: F 2600 mg/m^2 24h infusion, L 200 mg/m^2, and oxaliplatin 85 mg/m^2, every two weeks or FLP: F 2000 mg/m^2 24h infusion, L 200 mg/m^2, weekly, and cisplatin 50 mg/m^2, every two weeks. The primary end point was PFS (power, 80%; 1-sided log-rank test; significance level 0.05).
Results: 220 pts were randomized (FLO, 112; FLP, 108) between Aug 2003 and Jan 2006. Median age was 64 years and median ECOG was 1. Median treatment duration was 4.3 months with FLO and 3 months with FLP. FLO was associated with significantly less NCI-CTC grade 1−4 anemia (54% v 82%), nausea (57% v 71%), vomiting (37% v 52%), alopecia (22% v 39%), fatigue (20% v 36%), renal toxicity (11% v 34%), and serious adverse events related to the treatment (9% v 19%), and FLP was associated with significantly less peripheral neuropathy (25% v 60%). There was a trend toward increased median PFS with FLO versus FLP (5.7 months v 3.8 months, respectively), which did not reach the statistical significance (P=.0725). OS was 10.8 months for FLO and 8.7 months for FLP (NS). However, in pts aged >65 years (n = 94), treatment with FLO resulted in a significantly superior response rate (34.9% v 16.7%), time to treatment failure (5.4 v 2.1 months, p = 0.0001), and PFS (6.0 v 3.1 months, p = 0.021). These differences seemed also to result in an improved OS in elderly pts treated with FLO (13.8 v 7.3 months, p = 0.081). In contrast, there were no significant differences in young pts between arms concerning all efficacy parameter.
Conclusions: FLO reduced toxicity and, in elderly pts, improved efficacy as compared to FLP. This leads us to consider FLO for future studies in combination with targeted drugs to further improve the outcome of pts with gastric cancer.

3503 ORAL

Adding external beam to HDR-intraluminal brachytherapy, improves palliation of oesophageal cancer: a prospective randomized, multicentre trial of the International Atomic Energy Agency

E. Rosenblatt[1], G.W. Jones[2], R. Sur[3], B. Donde[4], J.V. Salvajoli[5], S. Ghosh-Laskar[6], A. Frobe[7], A. Suleiman[8], Z. Xiao[9], S. Nag[10]. *[1]International Atomic Energy Agency., Applied Radiation Biology and Radiotherapy., Vienna, Austria; [2]Credit Valley Hospital, Radiation Oncology, Mississauga, Canada; [3]McMaster University, Radiation Oncology, Hamilton, Canada; [4]University of the Witwatersrand Medical School, Radiation Oncology, Johannesburg, South Africa; [5]Hospital do Cancer AC Camargo, Radiation Oncology, São Paulo, Brazil; [6]Tata Memorial Centre, Radiation Oncology, Mumbai, India; [7]University of Zagreb, Radiation Oncology, Zagreb, Croatia; [8]Radiation and Isotopes Centre, Radiation Oncology, Khartoum, Sudan; [9]Chinese Academy of Medical Sciences, Radiation Oncology, Beijing, China; [10]Kaiser Permanente, Radiation Oncology, Santa Clara, USA*

Background: While the addition of oesophageal high dose-rate intraluminal brachytherapy (HDR-ILBT) has shown improved palliation compared with external beam radiation therapy (EBRT) alone, it is not known whether the addition of EBRT adds to the benefits of ILBT alone. This study aims at identifying resource-sparing treatment strategies to be adopted in low-income developing countries.
Methods: Patients were recruited in 6 countries where oesophageal cancer is common. Patients had localized non-metastatic, squamous-cell carcinoma, not amenable to curative therapy. They were managed with two ILBT of 8 Gy each, at 1 cm of the sources centres, and were randomized to EBRT of 30 Gy in 10 fractions vs. no EBRT. Worsening of dysphagia and the occurrence of a fistula were combined into a "dysphagia-free experience" (DFE) plot. Study endpoints were DFE, dysphagia score, ECOG performance status, quality of life and weight. Patient survival was not an endpoint in this study.
Results: 219 patients were randomized: 110 received EBRT and 109 did not. Patient characteristics, disease stage, symptoms and quality of life in both groups were similar. The main outcome of DFE was significantly improved with EBRT, by an absolute 18% (a sustained difference from 50 to 350 days of follow-up from randomization), with p = 0.019 by log-rank. Mean dysphagia scores were 0.79 with combined therapy and 1.23 with brachytherapy alone, a difference of 0.44 in favour of EBRT. Mean regurgitation scores were 0.36 and 0.72, respectively, a difference in favour of combined therapy. Adverse events were not different between the two study groups (e.g. perforations, ulcers). In particular, occurrences of strictures were in 5 cases with EBRT, and 1 without EBRT (p = 0.21), while occurrences of fistulae were in 12 cases with EBRT, and 7 without EBRT (p = 0.34); and the combined risks of either stricture or fistula at one-year were approximately 25% in both study groups. Overall median survival was 188 days; with no difference between study arms (p = 0.35). Performance status (an ECOG score difference of −0.40), and some quality of life measures ("activity level" and "feeling of well-being") were significantly improved with EBRT. Hierarchical multivariate analyses confirmed the findings regarding the benefits of combined therapy relative to brachytherapy alone.
Conclusions: The addition of EBRT to HDR-ILBT improves palliation in patients with squamous cell carcinoma of the oesophagus.

3504 ORAL

A randomized phase III study comparing gemcitabine monotherapy with observation in patients with resected pancreatic cancer

T. Kosuge[1], H. Ueno[2], Y. Matsuyama[3], J. Yamamoto[4], A. Nakao[5], S. Egawa[6], R. Doi[7], M. Monden[8], T. Hatori[9], M. Tanaka[10]. *[1]National Cancer Center Hospital, Hepatobiliary and Pancreatic Surgery Division, Tokyo, Japan; [2]National Cancer Center Hospital, Hepatobiliary and Pancreatic Oncology Division, Tokyo, Japan; [3]Tokyo University, Department of Biostatistics, Tokyo, Japan; [4]Cancer Institute Hospital, Department of Gastrointestinal Surgery, Tokyo, Japan; [5]Nagoya University, Department of Surgery II, Aichi, Japan; [6]Tohoku University, Division of Gastroenterology, Miyagi, Japan; [7]Kyoto University, Department of Surgery, Kyoto, Japan; [8]Osaka University, Department of Surgery and Clinical Oncology, Osaka, Japan; [9]Tokyo Women's Medical University, Department of Surgery, Tokyo, Japan; [10]Kyushu University, Department of Surgery and Oncology, Fukuoka, Japan*

Background: Gemcitabine (Gem) is considered to be a standard chemotherapy for unresectable advanced pancreatic cancer. However, the role of Gem in patients (pts) with resectable pancreatic cancer is uncertain. This study was designed to determine whether adjuvant chemotherapy with Gem improves the outcome of pts with resected pancreatic cancer.
Materials and Methods: This randomized phase III study was conducted at 10 centers in Japan. Eligibility criteria included gross complete resection of invasive ductal carcinoma of the pancreas and no prior radiation or chemotherapy. Pts were randomized to receive Gem monotherapy or observation using the minimization method stratified by pathological stage (UICC 5th edition stage I, II vs. III, IV), resection status (R0 vs. R1) and centers. Gem was administered at a dose of 1,000 mg/m^2 over 30 min on days 1, 8, and 15 every 4 weeks for 3 cycles. The primary end point was overall survival (OS), and secondary end points were disease-free survival (DFS) and adverse events.
Results: Between April 2002 and March 2005, 119 pts were entered into the study. Among them, 118 pts were eligible and analyzable (58 in the Gem arm, 60 in the observation arm). Both arms were well balanced in terms of baseline characteristics. Although hematologic toxicity was frequently observed in the Gem arm (grade 3 or 4 leukopenia 24.6%, grade 3 or 4 neutropenia 70.2%), most toxicities were transient, and grade 3 or 4 non-hematologic toxicity rarely occurred. During a mean follow-up period of 21.2 months, 42 pts (72.4%) in the Gem arm and 51 (85.0%) in the observation arm developed recurrent disease. Pts in the Gem arm demonstrated significantly longer DFS than those in the observation arm (median DFS, 11.44 months vs. 4.97 months; hazard ratio = 0.59 [95% confidence interval: 0.39−0.89]; P = 0.01). Also, the median OS of pts in the Gem arm was better than that of pts in the observation arm (median OS, 22.31 months vs. 18.36 months), although not to a significant degree (hazard ratio = 0.79 [95% confidence interval: 0.51−1.22]; P = 0.29).
Conclusions: Adjuvant chemotherapy with Gem significantly improved DFS compared with observation in pts with resected pancreatic cancer. OS was also more favorable in the Gem arm, although the difference did not attain statistical significance. We conclude that adjuvant chemotherapy with Gem may be considered as an optimal treatment in pts scheduled for resection of pancreatic cancer.

3505 ORAL

Glufosfamide (GLU) in metastatic pancreatic adenocarcinoma previously treated with gemcitabine: Results of a Phase III trial

V.K. Langmuir[1], T.E. Ciuleanu[2], A.V. Pavlovsky[3], G. Bodoky[4], A.M. Garin[5], S. Kroll[1], A.B. Colowick[1], G.T. Tidmarsh[1]. *[1]Threshold Pharmaceuticals, Clinical Affairs, Redwood City CA, USA; [2]Ion Chiricuta Cancer Institute, Medical Oncology, Cluj, Romania; [3]Central Research Institute of Radiology, Oncology, St Petersburg, Russian Federation; [4]St Laszlo Hospital, Medical Oncology, Budapest, Hungary; [5]Blokhin Cancer Research Center, Clinical Pharmacology and Chemotherapy, Moscow, Russian Federation*

Background: Glufosfamide is glucose linked to isophosphoramide mustard, the active metabolite of ifosfamide. Cancer cells use glucose at a higher rate than normal cells, which may lead to preferential metabolic targeting by GLU.
Methods: Patients (pts) with metastatic pancreatic adenocarcinoma previously treated with gemcitabine and with adequate KPS and renal (CrCL $\geqslant$ 60 mL/min), hepatic and hematologic function were randomized