showed any K-Ras mutations in the bile fluid. In contrast 17 (34%) of 50 patients with PSC revealed K-Ras mutations in the bile fluid. The Mayo-score of the PSC patients was not significantly different between the PSC-patients with (n = 15, score = 0.45) and the PSC-patients without (n = 27, score = 0.3) K-Ras mutations. In 6 of the 50 patients with PSC an orthotopic liver transplantation was performed. In 4 of the 6 patients a K-Ras mutation could be observed more than 12 months before OLT. The explanted livers were intensively investigated by a pathologist. The PSC livers without K-Ras mutations revealed only the typically inflammatory bile ducts of PSC. However in the group of the PSC-livers with K-Ras mutations one liver showed high graded dysplasia in the bile ducts and in two livers incidental cholangiocellular carcinomas could be observed. The K-Ras mutations of the bile could be confirmed in the tumors.

Conclusion: Our results suggest that the occurrence of K-Ras mutations is an independent prognostic factor for PSC-patients.

500 ORAL

A randomized trial on hepatic arterial CDDP and i.v. 5-FU in unresectable colorectal liver metastases

M. Cosimelli[1], M. Tedesco[1], R. Mancini[1], D. Giannarelli[1], C. Garufi[1], L. Tipaldi[1], E. Cortesi[2], P. Di Tora[3], L. Capussotti[4]. [1]*Regina Elena Cancer Institute, Multidisiplinary Colorectal Cancer Working Group, Rome;* [2]*University, Deparment of Medical Oncology, Rome;* [3]*Umiversity of Palermo, Deparment of Surgery, Palermo;* [4]*Mauriziano Hospital, Department of Surgery, Torino, Italy*

Following a previous phase II study on bolus hepatic arterial CDDP and i.v. 5-FU, this multicentric randomized phase II clinical trial was started to evaluate effectiveness to give hepatic arterial CDDP and i.v. 5-FU. Since the minimum follow-up is 36 months, long-term results are now available.

Material and Methods: One hundred twenty-three pts with colorectal liver metastases staged III and IV A according to the TNM classification modified by Gayowski and Starzl underwent surgical cannulation of gastroduodenal artery and port implantation. Hepatic arterial CDDP 24 mg/m^2/day by bolus (arm A) vs continuous (arm B) infusion and i.v. 5-FU 500 mg/m^2/day were delivered on days 1 to 5 every 28.

Results: Objective responses evaluated by liver sonogram were 52% and complete responders were 17 without significant differences between the two arms. The arm B experienced a lower number of toxic events; overall G3 toxicity was less than 30%. The 5-yr survival was 20.4 and 16.1 in the arm A and B respectively. The responders showed a 5-yr survival significantly higher than the non responders (28.2% vs 16.6%; p = 0.006). The complete responders experienced the highest survival (41.4%) and half of them benefitted by a surgical resection confirming a pathological response in 4 pts. In the arm B, the subgroup whit no change (30%) showed survival rates as high as the responders. All the pts with progression ab initio died within 14 months.

Conclusions: This combined hepatic arterial and systemic therapeutic approach allowed: a) to observe long-term survivors, b) to resect the complete responders, c) to reduce toxicity significantly when CDDP was delivered by continuous infusion.

501 ORAL

Basal level gene expression of thymidylate synthase (TS) in colorectal cancer and normal colon mucosa – No evidence of relation to disease course

P.-A. Larsson[1], E. Odin[2], Y. Wettergren[2], L. Larsson[2], G. Carlsson[2], B. Gustavsson[2]. [1]*Helsingborg Hospital, Dept. of Surgery, Helsingborg;* [2]*Sahlgrenska University Hospital/Östra, Dept. of Surgery, Göteborg, Sweden*

The aim of the present study was to prospectively analyse gene expression of TS as a prognostic factor in colorectal cancer. Biopsies were obtained from both tumour and macroscopically normal colon mucosa in 31 colorectal cancer patients. No patients were previously subjected to chemotherapy. Thirteen patients were classified as having advanced disease, i.e. tumours not amenable to curative resection at diagnosis or developing distant metastases or recurrent disease during the follow up period of 24 to 36 months. Eighteen patients were classified as having a locally controlled disease. The gene expression levels of TS were measured by semi-quantitative reverse transcription-PCR. Gene expression was calculated as the ratio between TS gene cDNA and beta actin cDNA × 10-2, quantitated on an ABI PRISM 7700 sequence detection system. Average TS gene expression was 98.3 ± 87.6 in tumor and 43.9 ± 25.7 in normal mucosa. Gene expression of TS was significantly higher in tumour biopsies than in normal colon mucosa ($p < 0.05$), but there was no significant difference in distribution of tumour TS values between patients with advanced disease and those with surgically controlled disease. Previous reports have suggested that high TS gene expression is associated with lack of response to 5-fluorouracil based chemotherapy and short survival. TS protein has also been proposed as an independent prognostic marker, but there is no evidence in the present study that high tumour TS gene expression predicts a more aggressive course of the disease.

502 ORAL

Value of peptide receptor imaging using indium-111-octreotide (OCT) and iodine-123 vasoactive intestinal peptide (VIP) in patients with carcinoid tumours: Vienna university experience 1993–1998

M. Raderer, A. Kurtaran, B. Niederle, F. Vorbeck, H. Vierhapper, W. Scheithauer, P. Angelberger, J. Pidlich, I. Virgolini. *University of Vienna, Internal Medicine I, Währinper Gürtel 18-20, A-1090 Vienna, Austria*

Introduction: Radioloabeled peptide analogs (111In-OCT, 123I-VIP) are being used to identify primary and metastatic tumour sites in patients with carcinoid tumours.

Methods: A total of 194 patients with a verified or suspected diagnosis of a carcinoid tumour were referred to our institution between 1993 and 1998. All patients underwent scanning with 111In-OCT, while 131 patients received both 111In-OCT and 123I-VIP in random order. Imaging results were compared to results to conventional staging including CT, sonnographyand endosonography not older than 4 weeks. In case of discrepancies, results of surgical exploration also were taken into account.

Results: In total, 84% primary or recurrent carcinoids could be visualized by means of 123I-VIP, while metastatic sites were indentified in 82% of patients. In patients scanned with 111In-OCT, 91% of primary or recurrent carcinoids could be identified, and metastatic sites could be imaged in 95%. In a direct comparison, 111In-OCT was found to be superior to 123I-VIP, with 93% vs 84% of scans being positive in primary of recurrent tumours, 90% vs 82% in metastatic sites, and 43% vs 25% in patients with carcinoid syndrome. Overall, peptide receptor scanning was more sensitive than conventional imaging, which located malignant lesions in only 71% of patients.

Conclusion: Our results indicate a high sensitivity for both peptide tracers for localizing tumour sites in patients with ascertained or suspected carcinoid tumours, with 111In-OCT scintigraphy being more sensitive than 123I-VIP receptor scanning. Both peptide tracers have a higher diagnostic yield than conventional imaging.

503 ORAL

Health-related quality of life in five-year survivors of endocrine gastrointestinal tumours

G. Larsson[1], P.O. Sjödén[1], K. Öberg[2], L. von Essen[1]. [1]*Uppsala university, Dep. of Public Health and Caring Sciences, Uppsala;* [2]*Uppsala university Hospital, Dep. of Endocrine Oncology, Uppsala, Sweden*

Purpose: Patients with endocrine gastrointestinal (GI) tumours have a relatively long median survival, those with carcinoid tumours, 90 months and those with endocrine pancreatic tumours (EPT), 72 months. In a mailed survey, HRQOL was evaluated in long-term survivors of endocrine GI tumours.

Methods: EORTC QLQ-C30, FACT-G and an importance-satisfaction with HRQOL aspects questionnaire were mailed to a sample of patients (carcinoid tumours n = 64, EPT n = 55) referred to the Dep.E.O., Uppsala University Hospital.

Results: Mean time since diagnosis was 130 months (range 60–360). All patients were still treated at the Dep.E.O. The majority of patients (77/119) had ongoing treatment (interferon, octreotid, chemotherapy, radiotherapy, omeprazol). Both the EORTC QLQ-C30 and the FACT-G ratings suggest that the patients perceive their HRQOL as relatively good. In addition, the ratings of satisfaction with selected HRQOL aspects indicate that quality of life was perceived as satisfactory. There were no major differences in the HRQOL ratings between patients with carcinoid tumours and patients with EPT. Patients who rated that a specific aspect was of a higher importance than their satisfaction with that aspect also rated a low HRQOL on the EORTC QLQ-C30 and/or FACT-G for that aspect.

Conclusion: In spite of a long disease duration and treatment, patients with endocrine GI tumours enjoy a good HRQOL as measured by the EORTC QLQ-C30 and FACT-G. The results suggests that discrepancies in the importance-satisfaction ratings of HRQOL aspects are valid indicators