in Mf, 59 in iceMFP) were excluded because of postoperative stage I in 90, IV (M1) in 13, positive resection margin in 10, and others in 6. Therefore, a total of 521 pts (258 in Mf, 263 in iceMFP) were eligible for intent-to-treat analysis. Postoperative stages were II in 33.4%, IIIA in 31.9%, IIIB in 17.5%, and IV in 17.3% of pts. With a median follow-up of 6.6 years, a total of 271 events (relapse or death) have been observed. As compared with Mf group, iceMFP group had a higher likelihood of relapse free survival (RFS) (HR, 0.73; 95% C.I. 0.57–0.93; p = 0.0092; 5yRFSR 53.9% vs 46.3%) and of overall survival (OS) (HR, 0.77; 95% C.I. 0.60–0.98; p = 0.0365; 5yOSR 59.2% vs 50.3%).
Conclusions: Considering no benefit of adding cisplatin and prolongation of oral doxifluridine to Mf chemotherapy in curatively resected AGC pts (AMC0201), intraperitoneal cisplatin and/or early start of chemotherapy seemed to be responsible for the improved efficacy of iceMFP chemotherapy in this study.

Poster Presentations (Mon, 26 Sep, 09:30−12:00) **Gastrointestinal Malignancies − Noncolorectal Cancer**

6506 POSTER

Tricellulin Expression in Normal and Tumorous Human Pancreas

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Background: Tricellulin (TRIC) is the first identified member of transmembrane tight junction (TJ) proteins, found concentrated mainly at tricellular contacts. However, together with occludin and claudins it can also be detected at bicellular junctions. TJs play essential role in cell adhesion as well as in the maintenance of paracellular barrier and are also involved in signal transduction. Further, altered expression of several TJ components was observed during carcinogenesis and tumour progression. Previously, our group described significant differences between exocrine and endocrine pancreatic tumours related to claudin expression. The aim of the present study was to analyze the expression and localization of TRIC in normal human pancreas as well as in exocrine and endocrine primary tumours of the pancreas.
Materials and Methods: A total of 82 cases were studied: 20 normal pancreas, 44 ductal adenocarcinomas (PDACs) (grade 1−3), 15 endocrine neoplasms (PENs) and 3 acinar cell carcinomas (ACCs). Fluorescent microscopic examination and Western-blot analysis were performed on fresh frozen samples, immunohistochemical analysis and RT-PCR on formalin-fixed, paraffin embedded materials. Data were analyzed by digital morphometry and evaluated statistically.
Results: TRIC was found apically localized in normal ducts and acini. Intensive, spotty immunopositivity was detected at tricellular contacts, while weaker signals were observed between two cells. Langerhans islets were negative. The appearance of TRIC in PDACs, however, was unorganized as compared with normal tissue. Well differentiated PDACs expressed TRIC at significantly higher levels compared with poorly differentiated adenocarcinomas. Kaplan-Meyer analysis showed significant correlation between survival and differentiation of PDACs and inverse correlation with TRIC expression. ACCs expressed TRIC in atypical, abortive acinar cells. All PENs were TRIC negative.
In conclusion, this is the first report to describe the TRIC expression profile in normal and neoplastic human pancreas. Both normal and tumorous pancreatic exocrine tissues expressed TRIC, whereas no expression was notable in the normal and tumorous endocrine cells. Further, TRIC expression in PDACs revealed significant negative correlation with the degree of differentiation and survival.
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6507 POSTER

Effects of the Proteasome Inhibitor Bortezomib Alone and in Combination With Chemotherapeutic Agents in Gastric Cancer Cell Lines

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The proteasome plays a pivotal role in controlling cell proliferation, apoptosis, and differentiation in a variety of tumour cells. Bortezomib is a boronic acid dipeptide derivative, which is a selective and potent inhibitor of the proteasome and has prominent effects in vitro and in vivo against several solid tumours. We examined the anti-proliferative and apoptotic effects of bortezomib in three gastric cancer cell lines (SNU638, MUGC-3 and MKN-28), along with its antitumour combination effects with other chemotherapeutic agents.
Tumour cell growth inhibition and apoptosis was measured by MTT assay and FACS analysis, respectively. Apoptosis- and cell cycle-associated protein expression levels were measured by Western blot assay. Bortezomib induced the suppression of tumour cell growth and apoptosis in a dose-dependent manner with an inhibitory dose (ID)50 of approximately 0.5 μg/ml in all gastric cancer cell lines tested. Further combination treatment with cisplatin and docetaxel, in particular with docetaxel displayed dramatically increased tumour cell growth suppression in all three gastric cancer cell lines, as compared to single drug treatment alone. This was concomitant with the induction patterns of apoptotic cells. Bortezomib treatment increased the Bax protein expression. Moreover, combination treatment of bortezomib plus docetaxel resulted in a dramatic increase in the Bax expression. In contrast, Bcl-2 expression was decreased by combination treatment with bortezomib plus docetaxel in SNU638 cells. Finally, bortezomib, docetaxel and to a greater degree bortezomib plus docetaxel increased the expression levels of p27 proteins even without influencing p53 expression levels. Bortezomib has profound effects on tumour cell growth inhibition and induction of apoptosis in human gastric cancer cells, suggesting that bortezomib may be an effective therapeutic drug for patients with gastric cancer. Further combination studies with other chemotherapeutic drugs, in particular docetaxel showing more tumour cell growth inhibition and apoptosis suggest that combining bortezomib with docetaxel might be more effective for displaying tumour cell growth inhibitory effects in gastric cancer cells through regulation of Bcl-2, Bax and p27 proteins in vitro.

6508 POSTER

A Case–control Study on the Effect of Apolipoprotein E Genotype on Gastric Cancer Risk and Progression

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Background: Apolipoprotein E (ApoE) is a multifunctional protein playing a key role in the metabolism of cholesterol and triglycerides as it mediates blood clearance of cholesterol-rich particles. ApoE gene (19q13.2) has three major isoforms encoded by ε2, ε3 and ε4 alleles with the ε4 allele associated with hypercholesterolemia and the ε2 allele with the opposite effect. An inverse relationship between cholesterol levels and gastric cancer (GC) has been previously reported, although the relationship between ApoE genotypes and GC has not been explored to date.
Since the question on the role of hypocholesterolemia as a predisposing factor, or result of the preclinical stage of GC itself, remains still under debate, our hospital-based case-control study aimed to overcome this issue by directly looking at the relationship between ApoE genotypes and GC, as well as the interaction with potential effect modifiers.
Materials and Methods: One hundred and fifty-six gastric cancer cases and 444 hospital controls were genotyped for *apoE* polymorphism. The relationship between GC and putative risk factors was measured using the adjusted odds ratios (ORs) and their 95% confidence intervals (CIs) from logistic regression analysis. A gene-environment interaction analysis was performed.

Table: Distribution of *ApoE* polymorphism among gastric cancer cases and controls

	Cases n (%)	Controls n (%)	OR (95% CI)[†]
ε3/ε3	109 (71.71)	253 (62.94)	1*
ε3/ε2 or ε2/ε2	15 (12.10)	68 (21.18)	0.40 (0.19–0.84)
ε3/ε4 or ε4/ε4	27 (19.85)	76 (23.10)	0.68 (0.36–1.26)

[†]OR adjusted by age, gender, alcohol consumption (as continuous variable), packyears of smoking, grilled meat consumption and familiy history of gastric cancer. *Reference category.

Results: Alcohol consumption was associated with an increased GC risk with ORs of 1.84 (95% CI = 1.10–3.07) and 3.29 (95% CI = 1.36–7.98) for moderate and heavy drinkers, respectively. A nearly doubled GC risk (OR = 1.95, 95% CI: 1.06–3.60) was detected among individuals smoking more than 25 pack-years. As shown in the table, a statistically significant 60% decreased GC risk (OR = 0.40, 95% CI: 0.19–0.84) was observed for those carrying at least one *apoE* ε2 allele if compared with