restriction fragment size was identified by horizontal electrophoresis. The survival was determined using Kaplan–Meier method, and the log-rank test was used for evaluation of differences in survival. The association between genetic factors and cancer risk were analyzed by logistic regression, and the results were expressed as odds ratios (OR) and 95% confidence intervals (CI). Statistical analyses were performed using CRAN 2.4.0 statistical software, and the decision on significance was based on $p < 0.05$.
Results: Comparison of allele distribution between PC patients and controls demonstrated that Val/Val genotype carriers in codon 432 CYP1B1 had lower PC risk of pancreatic cancer development compared wild type carriers (OR 0.59; 95% CI 0.36–0.96; $p = 0.035$). Heterozygotes also had lower risk (OR 0.69; 95% CI 0.49–0.97; $p = 0.033$). There was an even more signficant increase of risk in patients who had histologically verified PC. Variant allele in GSTP1 codone 105 was associated with a trend of higher PC risk (OR 1.38; 95% CI 0.96–1.97, $p < 0.05$). Increased PC risk was also observed for GSTT1deletion (OR 1.56; 95% CI 0.93–2.61, $p < 0.05$). The combination of GSTT1 mutation and GSTP1 deletion was associted with significantly increased PC risk (OR 2.5; 95% CI 1.20–5.20; $p < 0.05$). No significant association was observed between the polymorphism of other biotransforming genes and PC risk, and none of the gene polymorphisms investigated was associated with differences in PC survival.
Conclusions: Gene polymorphism of biotransforming genes may be associated with the risk of PC.

6614 POSTER

Clinicopathologic Significance of Expression of Nuclear Factor Kappa B and Its Target Gene Products in Gastric Cancer Patients

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Background: Nuclear factor-κB (NF-κB) is involved in cell proliferation, invasion, angiogenesis and metastases by activating or repressing NF-kB target genes. The principal objective of this study was to assess the prognostic significance of NF-κB and its target genes in gastric cancer.
Methods: The tumour tissues of 115 patients with gastric cancer were immunohistochemically evaluated using monoclonal antibodies against NF-κB. Preoperative serum levels of vascular endothelial growth factor (VEGF), interleukin-6 (IL-6) were assessed via Enzyme-Linked Immuno-Sorbent Assay (ELISA). C-reactive protein (CRP) and serum amyloid A (SAA) were measured via immunotrubidimetry.
Results: Positive rate of NF-κB was 42.6%. NF-kB expression was related to tumour size, depth of invasion, lymph node metastasis, stage, and lymphovascular invasion. NF-κB expression in tumour tissues was also related to serum levels of IL-6 ($p = 0.044$) and CRP ($p = 0.010$). IL-6, SAA, CRP were related to depth of invasion, VEGF and SAA were correlated with lymph node metastasis. IL-6, VEGF, SAA and CRP were related to the TNM stage. Univariate analysis demonstrated that immunostaining of NF-κB, levels of CEA, CA19-9, IL-6, VEGF, SAA were significantly related with both disease free survival and overall survival. Multivariate analysis verified that NF-κB (Hazard ratio: 3.40, $p = 0.024$) and SAA (Hazard ratio: 3.39, $p = 0.045$) were independently associated with overall survival.
Conclusions: Immunohistochemical staining of NF-κB expression was related to serum levels of target gene products. Serum levels of IL-6, VEGF, SAA, and CRP might be markers TNM stage. Increased expression of NA-κB and high levels of SAA were associated with poor overall survival in gastric cancer patients.

6615 POSTER

Derangement HNF4a Expression as a Candidate Marker of Hepatocellular Carcinoma Progression

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Hepatocyte nuclear factor 4 (HNF4)α is a nuclear receptor playing a key role in hepatic differentiation. This gene is transcribed from two distinct promoters, whose activity results in expression of two groups of isoforms and reflects the level of hepatocytes differentiation. HNF4αP2 isoforms are prevalent in embryonic liver, while HNF4αP1 become predominant in mature hepatocytes. According to our previous surveys, hepatocellular carcinoma (HCC) progression is associated with the deregulation of HNF4α. Investigations on the collection of chemically induced mouse HCCs of independent origin revealed strict correlation of HNF4α expression with tumour differentiation state. To examine whether alterations of HNF4α gene expression are representative for human primary liver tumours we have analyzed the synthesis of HNF4α isoforms in 37 cases of human HCC on the paraffin sections by immunohistochemical staining.
Intracellular localization and protein expression level of HNF4α isoforms were investigated immunohistochemically using specific antibodies for HNF4αP1 or HNF4αP2 groups of isoforms. HNF4α isoforms immunoreactivity was detectable in all studied tumours except few severely dedifferentiated cases. Nuclear staining of tumour cells with HNF4αP1 specific antibodies was less intensive than in normal hepatocytes. Activation of HNF4αP2 isoform, uncharacterisic for adult hepatocytes, was found in tumours (92% of cases) and surrounding liver tissue (56% of cases). We suppose that HCC progression is accompanied with activation of HNF4αP2 isoforms, decreased HNF4αP1 synthesis while in severely dedifferentiated tumours the expression of both groups of HNF4α isoforms is repressed. In order to investigate the possibility of using alterations in HNF4α isoforms expression as a prognostic factor for the HCC treatment, the pilot multifactor analysis of long-term survival after surgical HCC treatment were carried out. Maintenance of HNF4αP1 isoforms synthesis was found to be statistically reliable factor associated with overall survival. We expect that further analysis of correlation between tumour differentiation and patients postoperative survival rate with the pattern of HNF4α isoforms expression on the expanded collections of human HCCs archival samples would allow to estimate the possible impact of HNF4α expression analysis for HCC diagnostics and prognosis.
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6616 POSTER

Impact of Progression on Resource Utilization in the Treatment of NET

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Background: Neuroendocrine tumours (NET) are associated with high morbidity and mortality; however, literature on resource utilization with progression is scarce. The aim of this study was to compare resource use in advanced NET patients at diagnosis versus post-progression.
Materials and Methods: An online survey was administered to physicians in the US, UK, Germany, France, Brazil and Italy. The survey collected resource utilization during the baseline period (time post-diagnosis but pre-progression; 12.8 months), 1st (8.7 months), and 2nd progression (12 months). Progression was defined as measurable/ radiographic evidence of tumour progression.
Results: Of 4,100 surveys administered, 197 physicians participated (4.8%), providing data on 394 patients. NET subtypes included GI (45%), lung (24%), and pancreas (31%). Resource utilization consistently increased from baseline through progression (Table 1).

Table 1. Resource utilization at baseline vs. post progression

	Baseline			Any Progression*		
	All NET % (N = 377)	GI/Lung % (N = 264)	Pancreas % (N = 113)	All NET % (N = 640)	GI/Lung % (N = 442)	Pancreas % (N = 198)
Chemotherapy	21.8 (82)	23.9(63)	16.8 (19)	29.2 (187)	30.3 (134)	26.8 (53)
PRRT	1.9 (7)	1.9 (5)	1.8 (2)	6.1 (39)	6.3 (28)	5.6 (11)
Somatostatin analogs	61.0 (230)	61.7 (163)	59.3 (67)	48.0 (307)	48.4 (214)	47.0 (93)
Routine Monitoring						
Ultrasound	52.5 (198)	50.0 (132)	58.4 (66)	40.2 (257)	39.1 (173)	42.4 (84)
CT scans (conventional or helical)	84.9 (320)	86.4 (228)	81.4 (92)	81.6 (522)	82.8 (366)	78.8(156)
Other imaging†	49.6 (187)	48.1 (127)	53.1 (60)	34.4 (220)	33.5 (148)	36.4 (72)
Biomarkers	69.0 (260)	68.2(180)	70.8 (80)	55.2 (353)	54.1(239)	57.6 (114)
Lab tests	56.2 (212)	52.6(139)	64.6 (73)	46.9 (300)	43.4(192)	54.6 (108)
Visits (surveyed physicians)	97.1 (366)	96.6 (255)	98.2 (111)	96.3 (616)	95.7 (423)	97.5 (193)
Hospitalizations	37.1 (140)	36.0 (95)	39.8 (45)	43.9 (281)	43.0 (190)	46.0 (91)
Surgery	28.7 (108)	26.5 (70)	33.6 (38)	23.9 (153)	23.1 (102)	25.8 (51)
Targeted therapies Dagger;	1.3 (5)	1.1 (3)	1.8 (2)	3.9(25)	2.9 (13)	6.1(12)

*1st and assumed 2nd progression, potentially resulting in multiple events per patient.
† PET, SRS, mIBG, MRI, Chest X-Ray.
Dagger; Everolimus, sunitinib, imatinib, bevacizumab.

Conclusions: Recent recommendations propose that progression free survival should be the primary endpoint in clinical trials in NET. It is therefore important to characterize the impact that progression has in the