DHMEQ reduced viable cancer cells in the peritoneal cavity (CPM/mm^2 of DHMEQ treated group was reduced by 34.8±13.8%, while none of DMSO treated group reduced).
Conclusion: DHMEQ, by suppressing cancer cell proliferation and adhesion to peritoneum, may effectively prevent gastric cancer progression in abdominal cavity.

6636 POSTER

Genetic profiling of circulating tumor cells in the blood of patients with local advanced or metastatic upper gastrointestinal carcinomas

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Background: We have developed a new preanalytical enrichment method for circulating carcinoma cells (CTC) based on EpCAM and MUC1 specific antibodies coupled to immunomagnetic beads. Molecular detection and tumor cell characterization was performed with a multimarker panel by real-time RT-PCR. Here we present first results of a universal marker panel for upper gastrointestinal carcinomas (including carcinomas of stomach, duodenum, pancreas and biliary tract).
Methods: Samples from patients were divided in native probes and matched calibrator probes containing 2 and 10 carcinoma tumor cells (ETC). The high affinity antibodies BM7 (MUC-1) and VU1D9 (EpCAM) were used for immunomagnetic tumor cell enrichment from 10 ml peripheral EDTA-blood of patients with documented metastatic disease. Separated cells were lysed and used for mRNA isolation and c-DNA synthesis. Real-time quantitative RT-PCR approaches with SYBR assays (Eurogentec) and FAM-labeled TaqMan probes selected with the UniversalProbeLibrary system (Roche AG, Basel, CH) were developed for the epithelial markers cytokeratin19 and 20 (CK19/20), EpCAM, CEA, Survivin, CD276, metastasis associated in colon cancer (MACC) transketolase TKTL1 and HIF-1alpha.
Results: Sensitivity of the the multimarker panel was validated in calibration tests with 2 cells and 10 cells (embedded tumor cell calibrators, ETC) and the specificity of the panel was confirmed by examination of blood from healthy donors. Positivity rate of ETC controlled real-time RT-PCR on the basis of the multimarker panel was 71% (12 of 17 patients with local advanced and/or metastatic disease). 11 patients (65%) showed two or more positive markers. The marker with the highest prevalence was EpCAM (64%) followed by CK19 (43%), CD276 (43%), CEA (39%), Survivin (29%), CK20 (25%), MACC (14%).
Conclusion: We have used embedded tumor cells (ETC) as internal calibrators for accurate process control and normalization of the immunobead quantitative RT-PCR technique. The newly introduced surrogate marker panel from the networks of apoptosis, invasion, angiogenesis and stem cell phenotype should improve early detection of metastasis, monitoring of therapy response and efficacy and selection of tailored therapy regimes.

6637 POSTER

Expression of Bax predicts outcome in advanced gastric cancer patients treated with 5-fluorouracil, leucovorin, and oxaliplatin palliative chemotherapy

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Background: Platinum and 5-fluorouracil (5-FU)-based regimens have been used the most frequently in palliative chemotherapy for gastric cancer. The present study evaluated the prognostic significance of Bax, excision repair cross-complementation group 1 (ERCC1), and thymidylate synthase (TS) in advanced gastric cancer patients treated with 5-FU, leucovorin, and oxaliplatin (FOLFOX) palliative chemotherapy.
Materials and Methods: Seventy-two patients with metastatic or recurrent gastric cancer were treated with FOLFOX regimen. Pretreatment tumor biopsy specimens were analyzed for Bax, ERCC1, and TS expression by immunohistochemistry.
Results: High expression of Bax, ERCC1 and TS was observed in 31 (43%), 33 (46%), and 35 (49%) patients, respectively. The median overall survival (OS) of patients was 12 months. Low expression of Bax was associated with poor OS (median, 9 months vs. 18 months; 2-year, 10% vs. 48%; P = 0.0005) in univariate analysis, while expression of ERCC1 and TS was not correlated with patient outcome. In multivariate analysis, low expression of Bax was a significant independent predictor of poor OS (p = 0.029).
Conclusions: Low expression of Bax was significantly associated with the poor survival of patients with metastatic or recurrent gastric cancer treated with FOLFOX chemotherapy. Immunohistochemical staining for Bax with pretreatment biopsy specimen may be a useful in selecting FOLFOX regimen as a treatment option for advanced gastric cancer patients.

6638 POSTER

Significance of gene expression of vascular endothelial growth factor and its receptors in therapeutic effect of the hepatic arterial infusion chemotherapy against advanced hepatocellular carcinoma

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Background: Transcatheter arterial infusion chemotherapy using platinum complex was generally performed in patients with advanced hepatocellular carcinoma (HCC) but its prognosis was poor. Recently, it was reported that anti-angiogenic drug, sorafenib, was effective against advanced HCC. This drug is going to use together with anti-cancer reagents. In this study, gene expression of angiogenic factor (vascular endothelial growth factor (VEGF)) and its receptors (KDR and flt-1) was investigated and the relation between gene expression of them and therapeutic effect was investigated to assess any possibility of predicting the therapeutic effect.
Material and Methods: The subjects of this study were 37 HCC patients who received the chemotherapy with platinum complex by hepatic arterial infusion. After informed consent was obtained and prior to the start of treatment, liver biopsy was performed to collect tissue from the tumor site and non-tumor site. The expression amount of each gene was determined by quantitative PCR method using LightCycler. The amount of expression was expressed as a relative ratio to GAPDH.
Results: 1) The median follow-up duration was 9.7 months. The median survival time (MST) and 1-year survival rate were 9.6 months and 53%, respectively. Of 37 enrolled patients (male/female 34/3, median age 69 (range 46−75), Child-Pugh A/B 21/16 and portal vein invasion yes/no 9/28), one patient achieved complete response (CR) and thirteen patients achieved partial responses (PR) and eleven patients achieved stable diseases (SD) and twelve achieved progressive diseases (PD). The therapeutic effect was judged according to the RECIST criteria. 2) CR and PR cases were assessed as responders while SD and PD cases were assessed as non-responders. KDR expression in the former was significantly higher than the latter and VEGF expression in the former tended to be higher than the latter. 3) When the cut-off values were set at the median respectively and the patients were classified into the high expression group and low expression group, MST in the former was significantly longer in the latter in case of KDR (30.5 month/10.5 month, p < 0.05) but MST was no significant difference in case of VEGF and flt-1 respectively.
Conclusions: The substantial involvement of KDR is strongly suggested in predicting the effect of platinum-based chemotherapy and sequentially maintenance of VEGF signaling pathway may be prolonged survival.

6639 POSTER

Skeletal metastases in gastric cancer: analysis of skeletal-related events and plasma endothelin-1

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Background: Skeletal metastases occur approximately in 20% of patients with metastatic disease in gastric cancer. There have been limited reports that described skeletal-related events and their patho-physiologic mechanisms. Endothelin-1 (ET-1) and its receptors play an important role in the development of osteoblastic skeletal metastases, which have been investigated for prostate cancer. It has been reported that plasma ET-1 level is high in prostate cancer patients with skeletal metastases, suggesting its receptor antagonist would be a new therapeutic target. With regard to gastric cancer, ET-1 is not yet assessed for the clinical significance in the development of skeletal metastases.
Material and Methods: Between 2002 and 2008, we retrospectively reviewed the medical records of 85 patients with metastatic gastric cancer in our institute. Out of 108 patients, 19 patients (17%) were found to have skeletal metastases during their clinical course. They were analyzed