frozen tissue samples makes the TGA a useful system that can be widely applied in both diagnosis and research areas. We hypothesize that TGA is superior to DS for predicting efficacy of molecularly targeted agents, since it has greater sensitivity for detection of mutations associated with drug resistance.

1428 POSTER

Evaluation of EpCAM Protein Expression in Human Cancers as Therapeutic Target for Catumaxomab Treatment

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Introduction: The Epithelial Cell Adhesion Molecule (EpCAM) is a cell surface protein with oncogenic features expressed on healthy human epithelia and corresponding malignant tumours. Our work group recently explored molecular changes following EpCAM overexpression in commercially available cancer cell lines. For the first time we could show that EpCAM overexpression was associated with the downregulation of the Wnt signaling inhibitors. Moreover, an increase of proliferation and chemosensitivity to Docetaxel was associated with EpCAM overexpression. Similarly, in the clinical setting we observed that EpCAM overexpression detected by immunhistochemistry was associated with a poor prognosis in breast cancer patients and other tumour entities. These observations have promoted EpCAM to a 'druggable' target. As such, Catumaxomab was approved by the European Union for intraperitoneal use in patients with EpCAM-expressing cancer. However, no consensus exists on how and when to evaluate EpCAM expression in these cancer patients.
Material and Methods: EpCAM expression was assessed by a well established immunohistochemical staining protocol in 2291 primary tumour tissues and in 108 metastases using the EpCAM-specific antibody clone VU1D9. A total immunostaining score (TIS) was calculated as the product of a proportion score and an intensity score. Four expression subgroups (no, weak, moderate and intense) were defined. As described previously, the term 'EpCAM overexpression' was reserved for tissues showing a TIS-value >4.
Results: EpCAM was highly expressed in most tumours of gastrointestinal origin and in some carcinomas of the genito-urinary tract. However, hepatocellular carcinomas, clear cell renal cell cancer, urothelial cancer and squamous cell cancers are frequently EpCAM negative. EpCAM expression in breast cancer depends on the histological subtype, as lobular histology shows usually no or weak expression. Most metastases and particularly peritoneal lesions are EpCAM positive and they frequently reflect the expression phenotype of the primary tumour.
Conclusion: EpCAM expression is detected on adenocarcinomas of various primary sites. If EpCAM-specific antibodies (such as Catumaxomab) are intended to be used in cancer patients, we recommend prior immunohistochemical evaluation of EpCAM expression particularly in patients with renal cell cancer, hepatocellular carcinoma, urothelial carcinoma, breast cancer and squamous cell carcinomas.

1429 POSTER

FCGRIIa-131 and FCGRIIIa-158 Polymorphisms − Distribution and Clinical Outcomes of Cetuximab-based Chemotherapy in Japanese Patients With Metastatic Colorectal Cancer (mCRC)

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Background: Polymorphisms in fragment C receptor (FCGR) are expected as a predictive biomarker of cetuximab (Cmab). Previous studies have convincingly confirmed the distributions (dists) of FCGR polymorphisms in Western population and shown the existence of linkage disequilibrium (LD) between FCGRIIa and FCGRIIIa polymorphisms. Meanwhile, the dists in Asian population have been unknown but a few studies for non-cancer patients have suggested the difference in dists between Asian and Western populations. We investigated the dists of FCGR polymorphisms and their association with clinical outcomes of Cmab based chemotherapy in Japanese mCRC patients.
Materials and Methods: Ninety-three patients with irinotecan/oxaliplatin/5-FU-refractory mCRC and treated by Cmab plus irinotecan or Cmab monotherapy were retrospectively registered from 8 centers in Japan. FCGR polymorphisms were determined from genomic DNA extracted from peripheral blood samples based on the Multiplex allele-specific PCR method. Comparisons according to FCGR polymorphisms were evaluated using Fisher's exact test for response rate (RR) and log-rank test for progression-free survival (PFS) and overall survival (OS) curves.
Results: The dists of FCGRIIa HH/HR/RR and FCGRIIIa VV/VF/FF were 68/30/2% and 4/40/56%, respectively (Table). The absence of LD between FCGRIIa and FCGRIIIa polymorphisms was confirmed (GENEPOP, $p = 0.526$; Linkdis, $p = 0.146$). Of 74 patients with KRAS wild-type and treated by Cmab plus irinotecan, no difference according to FCGR polymorphisms was observed in either RR (IIa: HH 37% vs. HR/RR 36%, p=1.00; IIIa: VV/VF 39% vs. FF 35%, $p = 0.81$) or PFS curves (IIa: HH vs. HR/RR, $p = 0.60$; IIIa: VV/VF vs. FF, $p = 0.06$) or OS curves (IIa: HH vs. HR/RR, $p = 0.65$; IIIa: VV/VF vs. FF, $p = 0.30$).
Conclusions: This study clarified an ethnic difference in the frequencies of FCGR polymorphisms. The polymorphisms did not influence the clinical outcomes of Cmab based chemotherapy in Japanese patients with mCRC.

FCGRIIa-131	FCGRIIIa-158			
	VV	VF	FF	Total
HH	3	28	32	63 (68%)
HR	1	9	18	28 (30%)
RR	0	0	2	2 (2%)
Total	4 (4%)	37 (40%)	52 (56%)	93

1430 POSTER

Quantitative Analysis of PTEN-dependent Glycoprotein Patterns Reveals Predictive Biomarker Signature for Response of Human Patients to Docetaxel Therapy in Metastatic Castration Resistant Prostate Cancer (mCRPC)

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Background: Since 2004 chemotherapy with docetaxel has been the standard therapy in progressive mCRPC. Unfortunately only a subgroup of patients responds to this treatment. As rebiopsy is rarely done in mCRPC, predictive serum biomarkers for therapy response would be of great value. We recently presented a novel platform for human biomarker discovery and validation based on a large-scale quantitative analysis of *N*-linked glycoproteins of the Phosphatase and Tensin homolog (Pten) conditional knockout mouse model for prostate cancer progression. This work delivered biomarker signatures for PTEN-status, Gleason sum and diagnosis in localized prostate cancer (Cima et al., PNAS 2011). This model has also revealed a prognostic biomarker signature in patients with mCRPC (manuscript submitted). To screen our biomarker set for factors for response to treatment with docetaxel in mCRPC patients seemed a reasonable step towards the vision of a personalized cancer medicine.
Methods: In serum samples from 40 patients with mCRPC who underwent chemotherapy with docetaxel we measured 13 proteins with ELISA and 66 different proteins by selected reaction monitoring (SRM) mass spectrometry. Random forest algorithm was applied to establish a multifactor signature predictive for response. Therapy response was defined as at least stable disease biochemically (PSA increase <25% over baseline) and by imaging after three cycles of therapy with docetaxel.
Results: Serum samples of 40 patients with mCRCP under chemotherapy with docetaxel were retrospectively analyzed. We identified four factors correlating significantly ($p < 0.05$) with therapy response in a univariate analysis. Additionally we performed a random forest analysis identifying combined predictive biomarker signatures. Intriguingly the serum concentration of two identified factors in combination significantly predicted whether patients with mCRPC responded to taxane therapy or not with an accuracy of 85% in a confusion matrix.