[2] Aarøe J et al. (2006) The 97th AACR Annual Meeting, 1−5 April, USA.
[3] Aarøe J et al. (2006) The 19th EACR Conference, 1−4 July, Hungary.

1310 POSTER

Association of Her2Neu Ile655Val polymorphism with clinical characteristics, response to neoadjuvant chemotherapy and cardiac toxicity in locally-advanced breast cancer

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Background: Locally-advanced breast cancer (LABC) is a heterogeneous group requiring different treatments for disease control and enhancement of survival. The aims of our study were to evaluate the frequency of Her2Neu Ile655Val polymorphism in patients with LABC, and to study it's association with clinical characteristics, response to neoadjuvant chemotherapy (CT) and cardiac toxicity.
Methods: Women with LABC with or without her2Neu overexpresion (h2N-OE), who received neoadjuvant CT with FAC 4 cycles followed by paclitaxel (80 mg/m^2) for 12 weeks were included. Patients with h2N-OE received trastuzumab load dose of 4/mg/kg and 2 mg/m^2 weekly during neoadjuvant CT. HER2 polymorphism was determined by RFLP, using BsmA1 enzyme. Cardiac toxicity was measured with MUGA at baseline and at the end of treatment. The study was approved by local ethics committee.
Results:114 patients with LABC and 107 healthy controls were included, median age was 46.4±9, ER and PR positive were 46.5% and 24.6% respectively, h2N-OE 3+ or FISH+ was 43.9%. The frequency of Ile655Val in controls was of 20.6% and in LABC of 25.4% (NS). The patients who had h2N-OE presented the polymorphism in 36% vs 17.2% who did not (OR 1.6, CI 95% 1.1−2.7, p = 0.021). We did not find association between age, nodal status, clinical and pathologic response, nuclear grade and the polymorphism. In the HER2 subgroup we found a higher prevalence of cardiac toxicity (45% vs. 21% p = 0.05), in patients with genotype Ile/Ile, Ile/Val, Val/Val cardiac toxicity was 11/53 (21%), 4/10 (40%) and 1/1 respectively, being a trend (p = 0.09).
Conclusion: Patients with HER2/neu overexpresion and Ile655Val polymorphism might have more cardiac toxicity. The presence of Val allele may be can cause more aggressive tumors. The following study showed a little perspective to individualized treatment on a genomic alteration besides able to let known pharmagenomic of some drugs like trastuzumab in susceptible persons.

1311 POSTER

Quantitative analysis of Pten conditional knockout mouse proteome reveals significant prognostic biomarkers for survival in metastatic castration resistant prostate cancer (CRPC)

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Background: Men with metastastic CRCP have a poor prognosis with a median survival of 16 to 20 months. The course of the disease is heterogeneous. Nomograms based on clinical parameters are often weak in prognostic accuracy. Rebiopsy is rarely indicated in CRCP. Therefore serum biomarkers are on high demand. The purpose of this study was to identify novel biomarkers for survival in the serum of patients with CRCP based on a screen of the murine Pten-dependent glycoproteome.
Methods: We established a novel platform for human biomarker discovery and validation based on a large-scale quantitative analysis of *N*-linked glycoproteins of the Pten conditional knockout mouse model for prostate cancer progression. Quantitatively comparing the glycoproteome of mice with homozygous Pten deletion with the corresponding control animals led to the identification of 153 candidate biomarkers. In serum samples from patients with CRCP we tested candidate biomarkers with ELISA for prognostic significance in survival.
Results: Serum samples of 68 patients with CRCP were retrospectively analyzed. Survival in the specific context was defined as the time between onset of the castration resistant state and death. We identified several candidates as biomarkers for survival in Kaplan Meier Plots. Three biomarkers with best significance in the log rank test showed p-values between 0.004 and 0.02. PSA and PSA doubling time were not significantly correlated with survival in our collective.
Conclusion: Our newly established biomarker-platform derived from a Pten conditional knockout mouse model showed high feasiblity for the identification of biomarkers for survival in CRCP. As the course of CRCP is heterogeneous prognostic serum biomarkers are likely to be helpful in the planning and scheduling of the therapeutic follow up.

1312 POSTER

Catumaxomab therapy eliminates putative CD133+ EpCAM+ cancer stem celles from malignant ascites: data from a pivotal phase II/III study

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Background: Putative cancer stems cells (CSCs) are defined as "tumor-initiating cells" that have the capacity to self-renew and to give rise to the variety of differentiated cells found in the malignancy. The CD133 membrane glycoprotein represents a CSC marker that has been previously demonstrated to be capable of identifying a cancer initiating subpopulation in brain tumors, melanoma and EpCAM+ solid tumors. The trifunctional anti-EpCAM x anti-CD3 antibody catumaxomab efficiently eliminates tumor cells from the peritoneal fluid of malignant ascites (MA) patients as demonstrated in a pivotal phase II/III trial (Parsons et al., ASCO 2008). Here we report on the presence of CD133+/EpCAM+ putative CSCs in MA and, more importantly, on the elimination of this cell population from the peritoneal fluid of MA patients by means of catumaxomab therapy.
Methods: 18 CTX-refractory patients with MA caused by a variety of primary carcinoma diseases (i.e. ovarian, pancreas and gastric cancer) were analyzed for the presence CD133+/EpCAM+ cells in peritoneal fluids by means of CD133+/EpCAM+ double staining on cytospin preparations. Analyses were performed before, 2 days after the first and 1 day after the last catumaxomab infusion, respectively. Double stained cytospin preparations were evaluated with a computerized image analysis system.
Results: Before therapeutic intervention, CD133+/EpCAM+ cells were detected in the peritoneal fluids of 14 from 18 patients suffering from MA. After the 1st infusion of catumaxomab (10 μg), 9 of these 14 patients showed complete elimination of the CD133+/EpCAM+ cells. After 4 i.p. catumaxomab infusions (10 μg day 0, 20 μg day 3, 50 μg day 7 and 150 μg day 10) the CD133+/EpCAM+ cells were completely eliminated from the peritoneal fluids of all 14 MA patients.
Conclusions: In a preliminary monitoring study, putative CSCs (CD133+/EpCAM+) were present in peritoneal fluids of 78% of analyzed MA patients with different underlying primary tumor entities. Catumaxomab efficiently destroyed CD133+/EpCAM+ cells within peritoneal fluids of MA patients. Consequently, catumaxomab-based therapeutic measures may offer an additional treatment opportunity to eliminate CSCs in EpCAM+ malignancies.

1313 POSTER

Catumaxomab treatment reduces VEGF protein levels within malignant ascites: data from a pivotal phase II/III study

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Background: Treatment with the trifunctional anti-EpCAM x anti-CD3 antibody catumaxomab efficiently eliminates tumor cells from the peritoneal cavity (ASCO 2007, Jäger et al.) and led to clinically relevant prolongation of puncture-free survival (PuFS) in patients with malignant ascites (MA) in a pivotal phase II/III trial (ASCO 2008, Parsons et al.). As vascular endothelial growth factor (VEGF) levels are markedly elevated in MA in comparison to cirrhotic ascites the question was addressed whether catumaxomab treatment impacts the expression or accumulation of VEGF within MA. Here we report that in addition to tumor cell depletion, VEGF protein levels in MA significantly decreased upon catumaxomab therapy. We propose that the strongly correlated tumor cell elimination and reduced VEGF protein levels are causative for the prolonged PuFS of patients suffering from MA.
Methods: VEGF and total protein levels were measured by ELISA and BCA from MA supernatants before catumaxomab therapy, after the 1st infusion (10 μg;day 3) and after the 4th infusion (150 μg;day 11). Data were statistically analysed for the ratio of the VEGF protein concentration versus the total protein concentration for the MA treatment groups with ovarian (OC) or non-ovarian cancer (NC) as underlying disease and the corresponding control groups that received paracentesis only.