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Association Between Serum Adipokines Levels and Quality of Life in Advanced Non-small Cell Lung Cancer

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Background: Serum adipokines are produced by adipose tissue and have an important role in cancer cachexia. They have been studied in several cancer patients with cachexia, but have not been studied in patients with non-small cell lung cancer (NSCLC) for prognosis and quality of life. Therefore, the aims of the present study were to evaluate the association between serum adipokines (adiponectin, resistin, leptin and ghrelin) levels and prognostic factors and also quality of life in patients with NSCLC.
Methods: Sixty seven patients (42 pts with weight loss and 25 without weight loss) and 20 healthy subjects were included in this study. The clinicopathological features were recorded. Antropometrical, laboratory data and serum adipokines levels were measured. The evaluations of quality of life in both patients and healthy subjects were assesed by EORTC QLQ-C30.
Results: Serum albumin ($p = 0.01$), adiponectin ($p = 0.78$) and leptin ($p = 0.03$) levels were lower in the patients, whereas CRP ($p = 0.00$), LDH ($p = 0.01$), resistin ($p = 0.00$) and ghrelin ($p = 0.34$) levels were higher than the healthy subjects. In patients with weight loss, serum albumin ($p = 0.02$) and leptin ($p = 0.04$) levels were significantly lower and serum ghrelin levels were higher than patients without weight loss. We also found a significantly increased serum ghrelin levels in non-squamous histology ($p = 0.02$). On multivariate survival analysis, high LDH ($p = 0.01$), high ferritin ($p = 0.02$) and ghrelin levels ($p = 0.00$) had significant independent effects on disease progression. In EORTC QLQ-C30 assessments, there were significant correllations between the scores of low physical functioning, low role functioning, low cognitive functioning, high fatigue, nausea/vomiting, dyspnoea and pain and decreased albumin, increased LDH and ferritin levels in the patients. In addition, while low adiponectin level was correlated with high fatique and pain scores, increased resistin level was correlated with low global quality of life score, and also increased ghrelin levels were significantly associated with low role functioning and low cognitive functioning scores.
Conclusions: Our study showed that low leptin and high resistin and ghrelin levels were found in NSCLC patients. Adipokines, particularly ghrelin, may have an effect on progression. Also, the importance of serum albumin, LDH, CRP remained in NSCLC. There were significant differences in quality of life in the patient groups. Confirmation of the roles of adipokines in NSCLC with further studies is needed.

Poster Presentations (Sat, 24 Sep, 09:30−12:00)
Translational Research

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Trastuzumab Binds to HER2 Non-amplified Breast Cancer Cells and Induces ADCC

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Background: HER2 is over-expressed in approximately 25% of breast cancers. Trastuzumab is a monoclonal antibody used to treat HER2 positive (HER2 gene amplification/IHC 3+, >30% cells), but not HER2 "negative" (non-amplified/low expression) breast cancer. Abrogation of HER2 signaling through the PI3K/Akt and MAPK pathways and antibody-dependent cell-mediated cytotoxicity (ADCC) are two major mechanisms of actions of trastuzumab. A retrospective study on the NSABP B-31 adjuvant clinical trial suggested a possible clinical benefit for the addition of trastuzumab to chemotherapy in patients with HER2 "negative" disease. In this study we investigated the possibility that trastuzumab might induce ADCC against HER2 negative breast tumour cells.
Materials and Methods: HER2 protein levels were determined by ELISA in HER2 amplified (SKBR3, HCC1954) and non-amplified breast cancer cell lines (CAL-51, CAMA-1, MCF-7, T47D, EFM19, MDA-MB-468), and in tumour and autologous normal tissue samples from patients. Fluorescence microscopy was used to examine Q-dot-labelled trastuzumab bound to cell surface HER2. CD56+ natural killer cell-mediated ADCC was assessed in trastuzumab-treated, HER2 amplified and non-amplified breast cancer cell lines.
Results: HER2 protein levels were significantly lower in the HER2 non-amplified cell lines (6.2 ± 1.9 − 55.1 ± 23.4 pg/μg) than in the HER2 amplified cell lines (SKBR3 – 748 ± 296 pg/μg; HCC1954 − 511.3 ± 80.9 pg/μg), consistent with the levels of HER2 observed in the HER2 "negative" patient samples (3.8 ± 6.1 pg/μg – 61.5 ± 34.2 pg/μg). HER2 protein was undetectable in 12/15 normal autologous tissues. Using fluorescence microscopy we showed that trastuzumab can bind to HER2 on each of the breast cancer cell lines examined including the MDA-MB-468 cell line, which has the lowest levels of HER2. Trastuzumab induced a significant ADCC response in the HER2 positive HCC1954 and SKBR3 cell lines, and in five of the non-amplified, low HER2 expressing cell lines examined, but not in the MDA-MB-468 cell line.
Conclusions: Our results suggest that HER2 non-amplified breast cancer cells, with low but detectable levels of HER2 protein can bind trastuzumab and initiate ADCC and that there is a significant difference between HER2 expression in normal versus HER-2 "negative" tumour tissue. These results warrant further investigation of the ADCC response to trastuzumab, and other HER2 targeted mAb therapies, particularly in early stage HER2 negative breast cancer.

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Gene Signature of Bevacizumab Effects in Primary Breast Cancer

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Background: At today, no proven predictive biomarkers of anti-vascular endothelial growth factor (VEGF) therapies are available but the need of them is becoming critical. To determine the mechanisms of early anti-angiogenic tumour response might be the first step toward the identification of potential predictive biomarkers. Bevacizumab, a recombinant humanized monoclonal antibody targeting VEGF, was administered to previously untreated patients to evaluate its effects on gene expression.
Material and Methods: 73 patients (pts) with histological proven breast cancer were prospectively enrolled in IMAGING phase II clinical trial (ML22197) designed to determine molecular biomarkers for bevacizumab therapy. Bevacizumab (15 mg/kg) (C1) was administrated 3 weeks prior to the beginning of chemotherapy consisted of 4 cycles of docetaxel (60 mg/mq), adriamycin (50 mg/mq) and bevacizumab (15 mg/kg) every 21 days (C2-C5). Eco-guided tumour core biopsies were performed at the baseline (BL) and two weeks after bevacizumab treatment (C1). RNA was extracted from paired samples (BL and C1) and examined using an Affimetrix Exon 1.0 ST array. Analysis included differential gene selection methods as fold change and signature p-value filters of t-paired test correcting for multiple comparisons.
Results: At the time of the analysis, the accrual of this trial is completed but data of response are not yet available. Pts were age 29−70 (mean: 48) years, 58 (79%) and 15 (21%) clinical stage II and III, respectively. Differential gene expression analysis of 55 paired samples showed that 434 genes significantly changes (FDR < 0.01) after bevacizumab treatment. Using Gene Ontology (GO) pathway analysis, we identified 176 gene categories, the most notably involved in angiogenesis (including VEGF activity and Notch signaling), immune response (including lymphocyte mediated immunity and leukocyte activation) and cell death.
Conclusions: GO pathway analysis identified a number of gene categories influenced by bevacizumab administration. Our data confirmed the relevant role of bevacizumab in angiogenesis and showed new GO pathways involved in bevacizumab mechanism of action including the activation of immune response. This analysis might be an informative method for identifying new genes involved in response to bevacizumab and so to identify new potential predictive biomarkers for this treatment.

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EpCAM+ Tumour Cells Are Frequently Detected in Malignant Ascites Samples- Results From a Randomized Phase IIIb CASIMas Study

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Background: The epithelial cell adhesion molecule (EpCAM) is a tumour-associated marker frequently expressed on various carcinoma tissues. The