RANKL/OPG ratio was upregulated in patients with breast and lung cancer and tended to decline after treatment with zoledronic acid whereas patients with prostate cancer presented with elevated OPG levels that persisted after treatment. CTX levels were significantly reduced in the whole study population at the second compared to the initial measurement ($p = 0.003$). Decrease in TRACP-5b levels tended to correlate with reduced incidence of SRE (HR = 0.39, 95%CI: 0.14−1.10, $p = 0.076$) and the model fit was improved when Performance Status (PS) at diagnosis was added in logistic regression analysis ($p = 0.051$). Tumor type (lung or breast vs prostate) and PS (PS >2 vs 0 or 1) were the only significant predictors for recurrence and death and none of the bone markers was able to improve predictive value when added to the model.
Conclusions: The RANKL/OPG axis is upregulated in patients with breast and lung cancer metastatic to the skeleton and tends to normalize after treatment with zoledronic acid, as reflected by decrease in serum bone resorption markers. Marker level responses are not predictive for disease progression or survival.

1087 POSTER

Expression of angiogenic genes: prognostic marker in patients with early-stage non-small cell lung cancer (NSCLC)

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Background: NSCLC is a major cause of cancer-related death worldwide. The prognosis for lung cancer patients is poor with 5-years survival rates being less than 15%. It is known that angiogenesis is an essential event for solid tumour growth. Vascular endothelial growth factor (VEGF) family of ligand and receptors (VEGFR) are described as powerful angiogenic factors. VEGF ligands bound to their receptors at the membrane levels, gathering a cascade of intracellular events. Our objective was to evaluate the expression and prognostic significance of VEGFA and VEGFR1 determined by real-time PCR (RTqPCR) in resectable NSCLC patients.
Methods: We performed RT-qPCR analysis to assess the expression of VEGFA and VEGFR1 (FTL1) in 151 frozen lung cancer specimens from untreated NSCLC patients who had undergone surgical resection. For this purpose, RNA was extracted using Trizol® and RTqPCR was performed using TaqMan® probes. Relative quantification was calculated by Pfaffl formulae, using GUS-B (endogenous control gene) for normalization. We correlate the expression of both angiogenic genes between them and with survival variables. All statistical analysis were done using the SPSS 13.0 software.
Results: Our results show a strong positive correlation between the expression of VEGFA and VEGFR1 in tumour samples ($p < 0.000$, Spearman's test). When patients were grouped according to tumor size, there was a trend in the way that bigger tissues express relative higher amounts of VEGFA and VEGFR1 ($p = 0.000$). We used the median as a cut-off value for both variables, therefore, cases were scored as high (H) or low (L) according to this criteria. There were 71.5% (108/151) of concordant results (both variables H or L). Kaplan Meier plots show that the group of patients expressing high levels of VEGFA and VEGFR1 (HH) has a worse prognosis than the other groups (HL or LL). The median OS for the HH group was 24.27 months, compared with the 38.03 months for the HL + LL group.
Conclusion: Our results reveal that, in NSCLC tumour samples, there is a correlation between the expression of VEGFA and VEGFR1 mRNA. Bigger tissues express relative higher amounts of VEGFA and VEGFR1. In addition, determination of these two genes by RTqPCR would be a useful clinical test to assess prognosis in NSCLC, due to the fact that higher levels of expression of both genes correlates with shorter OS.

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Serum levels of vascular endothelial growth factor receptor 2 (VEGFR2): prognostic biomarker in advanced non-small cell lung cancer (NSCLC)?

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Background: An increase in VEGF expression in tumour or some blood compartments (i.e. serum or plasma) has been found in solid tumours of various origins. Several studies have suggested that ligands and receptors of the VEGFs/VEGFR system play an important role in tumour growth and is associated with metastasis and poor prognosis. The aim of our study was to investigate the usefulness of serum VEGFR2 quantification as a new biomarker in advanced NSCLC.
Material and Methods: We studied 106 healthy controls (c) and 462 advanced NSCLC patients (p) (stage IIIB and IV) treated with cisplatin and docetaxel. Blood samples were collected before chemotherapy and the serum levels of the VEGFR2 were determined by ELISA.
Results: In the NSCLC group, the median age was 59.9, range (31−80); 82% were males. The histological subtypes were: 31.4% squamous, 49.8% adenocarcinoma, 15.3% large cell and undifferentiated and 3.5% other. There was a significant difference in the serum levels of VEGFR2 between c and p (mean±SEM): 6318±152 ng/ml and 8373±120 ng/ml, respectively ($p < 0.0001$). On the other hand, we found no statistical differences according to sex, histology, or stage. The area under the ROC curve was 0.744 indicating that VEGFR2 is an adequate biomarker for the discrimination between c and p. Dividing the cohort in two subgroups according to VEGFR2 levels: high (>9473.9 ng/ml) and low ($\leqslant$9473.9 ng/ml), we found significant difference in terms of Time to Progression (TTP). Patients with higher levels of VEGFR2 had a median TTP of 204 days whereas in the group with lower expression the median was 164 days, ($p = 0.039$).
Conclusions: In advanced NSCLC, we found higher levels of soluble VEGFR2 in p than in c. There was a correlation between higher expressions of soluble VEGFR2 with better prognosis, in terms of TTP, therefore a more thorough understanding in the role of the serum quantification of this angiogenic receptor in advanced NSCLC p seems to be an important task.

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Does EGFR gene deregulation and PI3KCA mutations predict response to chemoradiation in squamous cell anal cancer (SCAC)?

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Background: Chemoradiation is the standard treatment for locally advanced SCAC, and complete response can been achieved in 75–85% of cases. A meaningful question is whether molecular markers might predict the response to chemoradiation. Preclinical and clinical studies in several cancers have demonstrated that EGFR and PI3K alterations may impair the efficacy of radiotherapy or, limited to PI3K, of fluoropyrimidines. We analyzed the frequency of EGFR gene deregulation and PIK3CA mutations in patients with locally advanced SCAC who underwent concurrent chemoradiation, and we matched the results to clinical outcome.
Methods: Patients who underwent split course of mitomycin and 5-fluorouracil continuous infusion with concurrent radiation (total dose 59.4 Gy in two steps with a gap of two weeks), were considered for analysis. The EGFR gene status was assessed by Fluorescent In Situ Hybridization, PI3KCA mutations by direct sequencing. Objective tumor response was evaluated by radiological and endoscopic methods; if indicated, a confirmatory biopsy was performed.
Results: Data of 20 patients were recorded. Seventeen patients (85%) achieved a complete remission after chemoradiation. The EGFR gene copy number gain was detected in 2/19 (10%) evaluable cases, but did not correlate with response. A PIK3CA point mutation was detected in 7/20 (35%) patients: 6 patients were responders, while 1 patient did not achieve a response.
Conclusions: PI3K pathway could play a key role in the development of SCAC.