magnetic particles-labeled with antibodies against epithelial markers (cytokeratin 7/8 or EpCAM) were used. Finally the disseminated tumor cells are detected using anti-cytokeratin 7/8/18/19 antibodies followed by microscopic visualization. Once detected, cells were citogenetically characterized by means of FISH, to detect described chromosomic aberrations for each tumor type using commercially avilable kits (Vysis®).
Results: The described methodology was able to detect epithelial cells disseminated in the blood of aproximately 50% of the patients, with cell numbers ranging from 1 to 16 cells, in 6−10ml of peripheral blood, and with an exceptional case of 100 disseminated cells in a prostate cancer patient. The neoplasic nature of the identified cells was verified through cytogenetic characterization, evidencing that both metastatic colorectal carcinoma and bone metastatic breast carcinoma cells show amplification of the ZNF217 (20q13) gene, which is implicated in the development and progression of the cancer. For disseminated prostate carcinoma cells ProVysión panel containing probes for LPL (8p22) and c-myc (8q24), demonstrated that these genes' loss and gain respectively characterised these patients' tumors. In patients bearing bone metastatic from lung cancer, LaVysion kit identified in the disseminated tumor cells amplifications in c-myc (8q24), and EGFR (7p12), whose amplification predicts good responses to Gefitinib (Iressa) or Erlotinib (Tarceva), and the 5p15 region. Finally, UroVysion kit, for the detection of aneuploidies in chromosomes 3, 7, and 17 and loss of the 9p21in disseminated urothelial carcinoma of the bladder cancer in blood.
Conclusions: The optimised methodology allows the detection and phenotipical and genotipical characterization of disseminated tumor cells in routine peripheral blood samples, offering additional information to empirically evaluate clinical prognosis and select the most efficient chemotherapy treatment, and providing a new tool for the post-surgical monitorisation of patients with solid tumors.

515 POSTER

Zoledronic Acid (ZOL) treatment may improve survival in patients with lung cancer and high baseline N-telopeptide levels: a multivariate Cox regression analysis

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Introduction: In recent analyses, high N-telopeptide (NTX) levels were reported to be an indicator of poor prognosis in patients (pts) with bone metastases. ZOL can reduce NTX levels in this setting, and exploratory analyses have suggested that ZOL treatment correlates with improved survival in pts with NSCLC and high baseline NTX. Therefore, we conducted a multivariate analysis of baseline variables and treatment to examine their correlation with survival outcomes in pts with NSCLC and high baseline NTX levels in a placebo (PLA)-controlled, randomized clinical trial of ZOL.
Material and Methods: Pts with solid tumors and bone metastases were randomized to either ZOL or PLA for up to 21 months. Survival was assessed in the subset of NSCLC pts who had high baseline NTX levels (⩾64 nmol/mmol). The effects of >20 baseline variables and treatment group on survival were evaluated in univariate and multivariate Cox regression analyses, and significant covariates ($P < 0.05$) were included in a reduced model. The relative risk (RR) of death and associated 95% confidence interval (CI) were calculated for each.

Variable	RR	95% CI	P
ZOL vs PLA	0.565	0.381, 0.840	0.0047
Narcotics (Y/N)	1.757	1.110, 2.780	0.0161
Impaired PS (Y/N)	1.941	1.158, 3.255	0.0119
[Leu] (% incr v med)	0.977	0.960, 0.995	0.0112

Results: Among NSCLC pts, the association between ZOL treatment and survival was significantly different for pts with high v low NTX ($P = 0.020$), with RR = 1.34 ($P = 0.205$) and RR = 0.67 ($P = 0.034$) for the normal and high NTX pts, respectively. Pts with NSCLC and high baseline NTX levels (n = 144; 65% men, 35% women) had a median age of 64 yrs, ~76% had experienced ?1 SRE, ~80% required narcotic medication, 15% had some impairment of performance status (PS) and most pts had lymphopenia (median, 14% lymphocytes [Leu]). Among these pts, variables that correlated significantly with survival outcomes included treatment group, FACT-G score, race, narcotic use, PS, and [Leu]. After a full multivariate analysis, 4 significant covariates emerged for the reduced model (Table).
Conclusions: This multivariate analysis determined the following variables to independently correlate with improved survival in NSCLC pts with high baseline NTX: no narcotic use, no impairment of PS, higher lymphocyte count, and ZOL treatment. This retrospective analysis suggests that ZOL treatment is an independent variable for improved survival compared with PLA in pts with NSCLC and high NTX levels, warranting further study in prospective trials.

516 POSTER

Cap43/NDRG1 is a molecular marker of angiogenesis and prognosis in cervical adenocarcinoma

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Background: Cap43/NDRG1 is a nickel- and calcium-inducible gene that has been recognized to play a significant role in metastasis and invasion, as well as in the primary growth of malignant tumors, possibly through its ability to induce differentiation. The majority of studies until now have suggested a negative correlation between Cap43/NDRG1 expression and cancer progression. However, this plausible role of Cap43/NDRG1 in preventing cancer progression has been shown to depend on the tissue of origin and the tumor type. The aim of this study was to investigate the association between Cap43/NDRG1 expression and angiogenesis (microvessel density) and other clinicopathological factor in cervical adenocarcinoma.
Methods: A retrospective review was conducted of the records of 100 women with FIGO clinical stage I-II cervical adenocarcinoma who underwent surgery. We evaluated Cap43/NDRG1 and CD34 expression in the resected specimens by immunohistochemistry.
Results: A significant association was found between the expression level of Cap43/NDRG1 in the tumor specimen and the microvessel density, histologic grade of the tumor, tumor diameter, stromal invasion, lymph vascular space invasion and lymph node metastasis. Kaplan-Meier plots demonstrated a clear influence Cap43/NDRG1 expression on the survival time. The median overall survival time was 54.1 months in patients with tumors showing low Cap43/NDRG1 expression, as compared with only 36.4 months in patients with tumors showing high Cap43/NDRG1 expression (log-rank test; $p = 0.0018$).
Conclusions: These results suggest that increased expression of Cap43/NDRG1 may be associated with angiogenesis and might be a poor prognostic factor in patients with cervical adenocarcinoma.

517 POSTER

Comparison of allelic polymorphisms of insulin receptor substrate-1 and leptin receptor in breast and endometrial carcinomas

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Background: Obesity and diabetes mellitus are among cornerstone endocrine risk factors for several malignancies. These two pathologies, however, are unequally associated with endometrial cancer (EC) and breast cancer (BC), with the prevalence of former in obese and diabetic population (Calle et al., 2003). The cause for such difference is not currently known, and it seems reasonable to assume that the explanation is in polygenic nature of the two malignancies. The aim of the present study was to evaluate the distribution of polymorphic genetic variants of insulin receptor substrate-1 (IRS1 Gly972Arg) and leptin receptor (LepR Lys109Arg and Gln223Arg) in BC patients in comparison to EC patients. Polymorphisms mentioned above are considered to be associated with higher incidence of diabetes or with excessive body weight (Salopuro et al., 2005) as well as with risk of BC (Slattery et al., 2006; Snoussi et al., 2006); similar investigations in relation to EC have not been performed.
Methods: The study included 407 females (average age around 60 years): 105 healthy women, 192 patients with EC and 110 with BC. Additionally, we included a separate group of those who underwent glucose oral loading test (n = 80) in the study. Genomic DNA was extracted from peripheral blood leukocytes. Genotyping of IRS1 and LepR polymorphisms was performed by allele-specific real time PCR.