with regard to the pool of healthy human oral mucosa from healthy donors. When comparing opposed lateral oral mucosa and leukoplakia from the same patient, 60% of samples showed higher EGFR expression in opposed lateral oral mucosa than in leukoplakia. This could be explained by the "field cancerization" hypothesis in oral cavity. Conclusions: Although it was previously demonstrated that EGFR was over-expressed in head and neck cancers these results confirmed that it is also up-regulated in more initial phases of the precancerous lesion. These results indicate that EGFR may contribute to carcinogenesis. Therefore EGFR could represent an attractive diagnosis factor in oral leukoplakias. Support: S. Díaz Prado is beneficiary of an Isidro Parga Pondal contract from Xunta de Galicia (Spain).

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combining epigenetic and metronomic chemotherapy is feasible and effective in chemotherapy refractory tumors

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Epigenetic treatment of human cancers, with histone deacetylas inhibitors (HDACi)has received much attention. Valproic acid (VPA) is a well known anti-epileptic with substantial HDACi activity. Combination with chemotherapy is widely started in phase I trials.

No experience exists on combining metronomic ('low dose -continuous') and epigenetic treatment in refractory tumors.

Patients and methods: From 15/8/2007 to 10/3/2008 we treated 15 patients who presented with refractory solid tumors, most 2nd to 5th line. All these patients had PS 0-2 and no end organ failure.. Median age was 72y (55-90y).Tumor types: breast 4, prostate 3, nsclc 1,sclc 1,melanoma 2, H&N 1,ovarian ca 2, cervical ca 1. Median number of prior CT regimens: 3. Patients received concomitant valproic acid 40mg/kg and paclitaxel 20mg/m² daily from Monday to Friday, 2-3weeks per month.

Results: Disease stabilisation was seen in 9 pts, with tumor marker decrease in 4. Two patients with melanoma had partial response and 4 pts progressive disease. There were 2 cases of febrile neutropenia and 2 patients needed transfusion. No other gr3-4toxicities

Conclusion:

1. combining metronomic and epigenetic treatment is feasible and has no prohibitive side effects
2. in a substantial amount of patients this leads to prolonged disease stabilisation and even decrease of Tumor markers. Many tumors remained stable for > 3months
3. The responses in melanoma patients are provocative and seem to confirm the in vitro data on the usefullness of combining epigenetic and angiogenic treatment in this tumor type
4. although febrile neutropenia did occur, it was mostly short lived, in patients with extensive prior chemotherapy

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Optimization of cancer vaccination schedule looking for better responses to EGF vaccine in NSCLC patients

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Purpose: An optimized schedule of EGF-based vaccine was performed to increase the immunological and clinical response in NSCLC patients.

Patients and methods: Twenty advanced NSCLC patients were immunized with 2 biweekly doses of an EGF-based vaccine (200ug/dose) before first line chemotherapy. One month after of platinum based chemotherapy (4 to 6 cycles), monthly vaccination were reinitiated. Toxicity and humoral EGF specific immunity was evaluated.

Results: Vaccination was safe and well tolerated. The antibody titres against EGF were significantly higher than the values obtained post chemotherapy in the previous phase II clinical trial (50ug/dose, initiated one month after chemotherapy). Serum EGF concentrations decreased to undetectable levels in all vaccinated patients. A higher number of patients (85%) showed an immunodominant antibody response against the loop B on the EGF molecule as compare to 46% showing this pattern with the previous schedule of treatment. The percentages of EGF/EGFR binding inhibition were higher and positively correlated to a high antibody response against the loop B. The overall survival was positively associated to high antibody titters after vaccination and showed a trend to increase with a high antibody response against loop B at 7 months post chemotherapy. Moreover, longer survival times were reached in the subgroup of elderly patients (more than 60 years old) as compared to the results obtained in the previous phase II trial.

Conclusion: The new changes on the vaccination schedule rendered both, an amplified antibody response and better survival times of NSCLC treated patients than in previous trials. Surprisingly, clinical benefits were obtained for elderly patients.

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Expression of CXCR7 in p-stage I non-small cell lung cancer increases the risk for postoperative recurrence at the distant site and correlates with poor disease free survival

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BACKGROUND: The expression of chemokine receptors has been implicated in metastatic bahavior in different models of cancer. In the present study, we evaluated which chemokine receptors are expressed in lung cancer cells, and whether the chemokine receptor expression is associated with clinical features in completely-resected non-small cell lung cancer (NSCLC).

MATERIAL and METHODS: We quantitatively examined gene expression of chemokine receptors (CCR1–11, CXCR1–7, XCR1, and CX3CR1) in 12 cell lines of lung cancer, and examined gene expression of CXCR3, CXCR4, and CXCR7 in surgical specimens resected from NSCLC patients. A total of 127 consecutive patients from May 2001 to December 2002 were included.

RESULTS: Quantitative real-time reverse transcription-polymerase chain reaction revealed substantial expression of CXCR3, CXCR4, and CXCR7 mRNA in all the NSCLC cell lines. The CXCR7 expression values in patients with squamous cell carcinoma were significantly higher than that with adenocarcinoma (P=0.009). In p-stage I NSCLC, CXCR4 and CXCR7 expression values in patients with postoperative recurrence at the distant site were significantly higher than those with no postoperative recurrence (P=0.003 and P=0.007, respectively). In p-stage II-III NSCLC, CXCR3 expression values in patients with postoperative recurrence at the local site were significantly higher than those with no postoperative recurrence (P=0.049). In p-stage I NSCLC, the 5-year disease free survival rate of high CXCR7-expressing patients (63.2%) were significantly lower than those of low CXCR7-expressing patients (84.8%) (P=0.033). On the other hand, there was no difference in the 5-year overall survival rate according to the CXCR7 expression status (P=0.243). According to the CXCR3 and CXCR4 expression, there was no difference in the 5-year disease-free survival rate and overall survival rate. A multivariate analysis confirmed that high CXCR7 expression was an independent and significant factor predicting a poor disease free prognosis in p-stage I NSCLC (P=0.041).

CONCLUSIONS: Higher levels of CXCR7 appear to be associated with postoperative recurrence at the distant site and poor disease free prognosis in patients with p-stage I NSCLC.

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Basaloid squamous cell carcinoma of the head and neck - A heterogeneous group with different cytokeratin immunoprofiles from conventional squamous cell carcinoma

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Basaloid squamous cell carcinoma (BSCC) is a rare high grade variant of squamous cell carcinoma (SCC) with distinct clinicopathologic characteristics. Its histogenesis is not fully understood, and has been suggested to be from a totipotent primitive cell in the basal cell layer of surface epithelium or in the proximal duct of secretory glands. Cytokeratin immunoprofiles of BSCC have been reported in only a small number of cases, with variable results. Eighteen new cases of head and neck BSCC in 10 year period of Asan Medical Center, Seoul, Korea were subjected to immunohistochemical study for cytokeratin (CK) subsets (CK5/6, CK7, CK19) using tissue microarrays. CK5/6, a basal cell marker, was expressed in 14 cases (78%), and CK7, a ductal marker, in 6 cases (33%), while CK19, a squamous epithelial marker, only in 4 cases (22%). Based on the CK immunoprofiles, BSCC could be classified as basal (11), ductal (3), mixed (3), and null (1) phenotypes. The heterogeneous CK immunoprofiles of BSCC suggests complex pathogenesis and clinical behavior. The phenotypes, however, were not correlated with patient age (32-72), gender (14 males; 4 females), tumor location (5 larynx; 5 hypopharynx; 3 oropharynx; 1 nasopharynx; 1 nasal cavity; 1 maxillary sinus; 1 external auditory canal; 1 salivary gland), tumor morphology (presence of nuclear palisading; comedonecrosis; cribriform pattern; glands; mucin; desmoplasia; combined SCC), or clinical outcome (10 deaths; 2 diseases; 6 no evidence of diseases) in this study. The present immunohistochemical results are interesting to demonstrate a group of ductal phenotype, which