similar for all three of them (about 0.8 kg of muscle/3 months). Loss of adipose tissue was associated to progressive disease. The pathways between these 3 drugs and body composition changes remain to be investigated.

7159 POSTER

Mutations in FGFR3 and Ras in Urothelial Cell Carcinomas of the Bladder − No Association With MAPK Pathway Activation

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Background: Different members of the PI3K-AKT pathway (*PIK3CA, PTEN, TSC1, AKT1*) are altered in bladder cancer. *FGFR3* mutations characterize the superficial/papillary low-grade tumours and *RAS* genes are mutated in about 13% of all bladder tumours. Interestingly, mutations in *FGFR3* and *RAS* are mutually exclusive in bladder cancer.
Material and Methods: We have analysed the prevalence of somatic mutations in *FGFR3, KRAS*, *HRAS* and *BRAF* genes in 88 Urothelial Cell Carcinomas (UCC) (Parc de Salut MAR Biobank of Barcelona, Spain), and the immunohistochemical expression of phospho-ERK1/2 (Cell Signaling Technology, Beverly, MA) in 80 UCC. The association of these alterations with the pathological features of tumours was also investigated.
Results: About 56% of tumours were mutated, 40 (45.5%) in *FGFR3* and 9 (10.2%) in *RAS* genes (*KRAS* n = 6, *HRAS* n = 3). None of the tumours presented mutations in *BRAF* and there were no $FGFR3^{mut}$-RAS^{mut} combinations. $FGFR3^{mut}$ genotype was associated with low grade bladder tumours (WHO 2004) and according to the three-tiered classification (WHO 1999) grades 1 and 2 tumours did not show statistically significant differences in the percentage of *FGFR3* mutations. *RAS* mutations were not associated with any of the tumour groups. Fifty-six per cent of tumours showed high levels of pERK1/2. There was a marginal association between pERK1/2 overexpression and high grade and stage tumours. Wild-type tumours presented a significantly higher pERK1/2 expression and only *RAS* mutated tumours showed a weak increase in pERK1/2 expression.
Conclusions: Mutations in *FGFR3* characterize low grade bladder tumours (WHO 2004) and with regard to *FGFR3* mutations, grade 2 (WHO 1999) cases are more similar to low grade than to high grade UCCs. *FGFR3* mutations cannot activate MAPK pathway, so other genes different from *FGFR3* may be related with the pERK activation in bladder tumours.
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7160 POSTER

MicroRNA Profiling in Peripheral Blood Predicts Major Response to Sunitinib in Metastatic Renal Cell Carcinoma

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Background: Sunitinib is a standard therapy for metastatic renal-cell carcinoma, but markers to predict drug benefit are needed. In this study, we applied high-throughput microRNA (miRNA) expression profiling in peripheral blood samples to identify predictive markers.
Material and Methods: This multicentre prospective study included patients with clear-cell metastatic kidney cancer and no previous systemic therapy. Peripheral blood samples were taken before initiation of therapy and 2 weeks later. Patients received sunitinib 50 mg/day for 4 weeks every 6 weeks. RECIST criteria were followed to asesss response. Total RNA was isolated from peripheral blood samples and miRNA profiling was performed using microarrays. Patients were stratified according to time to progression of disease. Those with progression before 6 months were included in the “Poor response” group, patients with progression after 18 months were included in the “Prolonged response” group and the remaining patients in the “Moderate response” group. Boosting was applied to filter miRNA expression data according to progression results. Predictive models were built independently for “Poor Response” and “Prolonged response” using binary logistic regression. Predictive accuracy for calibration and discriminant power of predictive models were evaluated.
Results: At the time of the analysis, 44 patients were enrolled and 37 were available for response. Median age was 62, 78% of patients had prior nephrectomy and median follow-up was 9 months. There were 4 complete and 13 partial responses, whereas disease remained stable in 9 (>6 months in 6 of them) and progressed in 11. miRNA profiling of peripheral blood samples showed that 29 miRNAs were differentially expressed between patients in the Poor response group vs. the other groups, and 13 miRNAs were differentially expressed between patients with Moderate response vs. those with Prolonged response. Several predictive models comprising different miRNA sets were generated and evaluated. Differential expression of miR-30b*, miR-370, miR-31, miR-196b, miR-1285 and miR-196−3p was consistently associated with response, so these can be considered relevant biomarkers for sunitinib response.
Conclusion: miRNA profiling in peripheral blood may be a reliable way to identify biomarkes related to sunitinib benefit in patients with metastatic renal-cell carcinoma. Validation of predictive models is ongoing.

7161 POSTER

Prognostic Factors in Patients With Advanced Renal Cell Carcinoma

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Background: Besides to the classical clinical and analytical prognostic factors of advanced renal cell carcinoma (RCC), the prognostic significance of molecular markers and other analytical variables such as one of the actual pathways in the investigation of advanced RCC are also being analysed, although they have not been yet validated for their application in the regular clinical practice.
Materials and Methods: A retrospective cohort of 135 patients with advanced RCC treated with biological agents and/or cytokines (CK) was analysed between July 1996 and February 2010. The expression of several biomarkers by immunohistochemistry and 2 analytical variables were analysed and were correlated with prognosis.
Results: 67 patients were treated only with biological agents and 68 with CK (23 received also biological agents in a sequential manner). The univariate statistical analysis showed that the enhanced expression of HIF-1α correlated with a poor prognosis in patients treated with biological agents (PFS 5.4 vs 13.5 months with low expression, $p = 0.033$) including sunitinib (PFS 5.4 vs 13.4, $p = 0.001$) and CK (PFS 3.3 vs 5.7, $p = 0.003$). The overexpression of CAIX was associated to a better prognosis in patients that received biological agents (PFS 18.3 vs 5.2 months with decreased expression, $p < 0.001$; OS 32.1 vs 7.8, $p < 0.001$) including sunitinib (PFS 16.8 vs 5.5, $p < 0.001$), sorafenib (PFS 8 vs 3.5, $p < 0.001$) and CK (PFS 6.3 vs 2.7, $p = 0.003$; OS 32.9 vs 5.9, $p = 0.001$). Positive PTEN was related to a good prognosis in patients treated with sunitinib (PFS 15.1 vs 6.5 months with negative PTEN, $p = 0.003$) and CK (PFS 7.5 vs 3.8, $p = 0.037$; OS 13.7 vs 7.9, $p = 0.039$). The increased expression of p21 was related to a poor prognosis in patients that received biological agents (PFS 5.9 vs 16.8 months with high expression, $p = 0.024$) including sunitinib (PFS 6.2 vs 18.9, $p < 0.001$), sorafenib (PFS 4 vs 9, $p = 0.013$) and CK (PFS 3.9 vs 7.5, $p < 0.001$). Thrombocytosis was related to a poor prognosis in patients treated with biological agents (OS 15.9 vs 26.7 months without thrombocytosis, $p = 0.007$) and CK (PFS 2.6 vs 5.1, $p = 0.017$; OS 5.9 vs 14.3, $p = 0.010$). Neutrophilia was related to a poor prognosis in patients that received biological agents (OS 17.6 vs 25.4 months without neutrophilia, $p = 0.063$) and CK (PFS 2.6 vs 5.7, $p = 0.019$; OS 5.9 vs 12.8. $p = 0.035$). In the multivariate analysis, the overexpression of CAIX was a favourable prognostic factor independent of PFS with a HR of 0,107 ($p < 0.001$) and OS with a HR of 0,055 ($p < 0.001$).
Conclusions: Our experience has suggested the utility of de HIF-1α, CAIX, PTEN, p21, thrombocytosis and neutrophilia as prognostic factors in patients with advanced RCC. CAIX has shown to be an independent prognostic factor.