Some of the panel's preferences and interpretations were seen to be interesting in light of variations from existing Phase III data in some areas. Two such examples were

- Sunitinib or pazopanib or sorafenib were all considered appropriate treatments for patients with metastatic disease who have received prior cytokine therapy
- In nephrectomised patients with metastatic disease and no prior systemic therapy, sunitinib or pazopanib were considered appropriate in all prognostic groups, bevacizumab was considered appropriate only in low/intermediate risk patients and temsirolimus was considered appropriate only in high risk patients.

Conclusions: Differences in opinion could be looked at as areas for further research. Areas where the agreed opinion differs from existing phase III data could have been due to the influence of the results of phase II and other non-randomised studies. Expert opinion may be useful in difficult areas where the data is either absent or sparse. Potential use of this data to generate clinical neural networks that can be used as learning tools is being evaluated.

7115 POSTER DISCUSSION

ABCB-1 and VEGFR-3 Single Nucleotide Polymorphisms (SNPs) and Outcome on Sunitinib (SUN) Treatment in Metastatic Clear Cell Renal Cell Carcinoma (RCC)

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Background: SUN is an oral angiogenesis inhibitor targeting VEGFR-1, -2, and -3, PDGFR-α and -β, RET and c-Kit, approved for the treatment of advanced RCC. Reliable biomarkers predictive for SUN sensitivity or primary/secondary resistance to SUN are lacking.
Methods: We analyzed 15 SNPs in 6 genes (VEGF-A, VEGFR-2, VEGFR-3, CA-9, ABCB-1 and NR-1/3) on 80 fresh frozen clear cell RCC nephrectomy specimens (in 49 patients (pts) on normal kidney tissue, in 31 pts on tumour). After nephrectomy, all the pts were treated in the metastatic setting with SUN as first line anti-angiogenic therapy.
Results: Global median time-to-progression (TTP) was 13.5 months (mo) and global median overall survival (OS) 28.5 mo.
Pts with the TT/TA genotype of the missense rs2032582 SNP (2677G > T or G > A) in the ABCB-1 gene, responsible for drug transport, had a significantly worse outcome than pts with the GT/GA or GG genotypes. TTP was 9.0 versus 16.0 mo ($p = 0.03$) and OS 22.8 versus 31.0 mo ($p = 0.02$) respectively. The TT-variant of the synonymous rs1128503 SNP (1236T > C) was linked to a significantly worse outcome than the CT or CC genotypes. TTP was 9.0 versus 16.0 mo ($p = 0.03$) and OS 22.8 versus 31.0 mo ($p = 0.05$) respectively. No significant link with TTP/OS and the synonymous rs1045642 SNP (3435C > T) in ABCB-1 could be observed.
Pts with the GA variant of the missense rs307826 SNP (1480A > G) in the VEGFR-3 gene, responsible for tumoral angiogenesis and blocked by SUN, had a TTP of 9.3 mo ($p = 0.009$) and an OS of 15.0 mo ($p = 0.009$) versus 18.5 and 31.0 mo for pts with the wild type/wild type AA genotype. For pts with the GT variant of the missense rs307821 SNP (3971G > T), TTP was 10.0 mo ($p = 0.08$) and OS of 15.0 mo ($p = 0.15$) versus 16.0 and 30.7 mo for pts with the wild type/wild type GG genotype.
We did not observe any link between TTP/OS and SNPs in the following genes: VEGFR-2 (rs1870377, rs1870378, rs1870379), CA-9 (rs1538536, rs1934158, rs12553173, the latter a prognostic factor for OS in immunotherapy with interleukine-2), VEGF-A (rs699947, rs2010963) and NR-1/3 (rs4073054, rs2307424).
Conclusions: We observed significant associations between SNPs in genes involved in drug transport (ABCB-1) and in tumoral angiogenesis (VEGFR-3) and response on SUN in advanced clear cell RCC pts.

Poster Presentations (Sun, 25 Sep, 14:00–16:30)
Genitourinary Malignancies – Other

7116 POSTER

Influence of BIRC5 −31G/C Polymorphism in Renal Cell Carcinoma (RCC) Development and Metastization

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Background: Renal cell carcinoma (RCC) is a heterogeneous group of tumours which represents about 3% of all tumours in adults. Furthermore, considering only urological tumours, CCR is the most common tumour after prostate carcinoma and bladder cancer. The mechanism by which a normal cell progresses to a carcinoma, usually involves the disruption of critical molecular pathways, like apoptosis. Alterations in gene expression involved in apoptosis are thus likely to contribute to cancer risk. Survivin, encoded by the *BIRC5* gene, is a multifunctional protein involved in inhibition of apoptosis and regulation of cell cycle. *BIRC5 −31G/C* is a polymorphism in the promoter region, responsible for a G-to-C substitution at −31. This transition has been associated with overexpression of survivin, which may overcome an apoptotic checkpoint and favour aberrant progression of tumour cells through mitosis. Therefore, the purpose of this study was to investigate the role of *BIRC5 −31G/C* polymorphism in RCC development.
Material and Methods: DNA was extracted from peripheral blood cells of 744 individuals: 178 patients with histopathologic diagnosis of RCC and 566 healthy individuals without evidence of neoplasic disease. Genotyping of *BIRC5 −31G/C* polymorphism was obtained by PCR-RFLP. The odds ratio (OR) and its 95% confidence interval (CI) were calculated as a measure of the association between *BIRC5 −31G/C* genotypes and RCC risk.
Results: Statistically significant differences where found between the control and RCC patients groups. Individuals carriers of the CC genotype present a higher risk for RCC development (OR=1.98, 95% CI=1.13–3.49, $p = 0.011$). Stratification according to lymph node metastasis and Fuhrman grade showed that carriers of CC genotype had an increased risk for being diagnosed with lymph node metastasis and higher Fuhrman grade (G1*vs*G2–4) when compared with G allele carriers (OR= 1.89, 95% CI=1.11–3.21, $p = 0.012$; OR=1.77, 95% CI=1.02–3.05, $p = 0.028$, respectively).
Conclusions: Genetic variants in germinal cell line can modulate the cellular microenvironment and consequently influence the molecular mechanism of CCR carcinogenesis. Our results suggest that *BIRC5 −31G/C* genetic polymorphism influence RCC risk and metastasis. This genetic profiling may help to understand RCC behaviour and to define high risk groups and to design new target therapies.

7117 POSTER

Claudins and Ki-67 – Potential Markers to Differentiate Low and High Grade Transitional Cell Carcinomas of the Urinary Bladder

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Background: Updated classification of urothelial cell cancer differentiates low grade and high grade cancers, which determines the potential clinical outcome. However, substantial interobserver variability necessitates new biomarkers to ensure classification. Claudins have been indentified as integral membrane proteins of tight junction strands and their specific expression pattern characterizes normal tissues, different tumour types and defined grades of tumour differentiation. Our aim was to examine expression pattern of claudins and the proliferation marker Ki-67 in low grade and high grade urothelial cell cancers compared with independent control samples of non-tumorous urothelium. Further, to reveal predictive usefulness of claudins.
Materials and Methods: The expression of claudins-1,-2,-3,-4,-5,-7,-10 and Ki-67 was studied with quantitative immunhistochemistry and real time RT-PCR with relative quantification in 103 samples: 86 urothelial cell cancers (27 low grades, 59 high grades) and in 17 non-tumorous urothelia. The results were analyzed regarding overall survival and recurrence-free period as well.
Results: High grade tumours overall showed significantly higher claudin-4 and Ki-67 and significantly lower claudin-7 expression when compared with low grade ones. However, high claudin-7 but not high Ki-67 expression was