was median 23 days (range 12−54) for both cycles. The recovery time was median 10 days for neutrophils and 11 days for platelets in both cycles.
Conclusions: The SWENOTECA IV HDCT strategy resulted in a favorable outcome within a population-based cancer care program. Furthermore, toxicity and hospitalization did not differ between the first and the second HDCT cycle.

7112 POSTER DISCUSSION

Early Diagnosis of Androgen Deprivation Syndrome in Testicular Cancer Survivors − an Audit of 1155 Patients in the West Midlands

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Background: Testicular cancer (TC) is a curable malignancy in the majority of the patients. A minority of TC survivors develop androgen deprivation syndrome (ADS) with vague symptoms that are not always appreciated. This study refers to TC survivors in the West Midlands, who were diagnosed with ADS and started with androgen replacement treatment (ART) at the University Hospital Queen Elizabeth Cancer Centre.
Materials and Method: The details of patients started on ART during the last 11 years were retrieved from the disease specific data-base and cross-matched with the hospital records. For each patient, we recorded the following: Demographics, age at diagnosis, single or bilateral orchidectomy, site and stage at presentation, histology, treatment details, relapse, Testosterone/FSH/LH assessment, date of first reported symptom, type of symptoms, time interval since diagnosis, time Interval between 1st symptom and 1st prescription of ART, age at 1st prescription, type and efficacy of ART.
Results: A total of 88/1155 (7.61%) patients with history of TC were started on ART during the last 11 years at the QE cancer Centre. The majority of patients (82/88) were diagnosed with ADS since 2006 as the level of clinical suspicion and vigilance increased. The median age of patients who were offered ART was 39 yrs (min 17, max 74). Patients with bilateral orchidectomy (BO:40/88) were started at the time of 2nd surgery before they developed symptoms. Patients with single orchidectomy (SO:48/88) reported at least 1 of the following prior to ART: lethargy 43/48, loss of libido 33/48, shaving pattern change 20/48, other: weight gain 4/48, mood change/depression 3/48, and headaches 3/48. The median level of Testosterone before ART was 8 nmol/L (range 0.5−23 nmol/L). The majority of patients had elevated LH/FSH prior to developing symptoms. The majority of patients (38/48, 79.1%) had clinical benefit from ART. None of the patients has been diagnosed with prostate cancer so far.
Conclusion: ADS is an under diagnosed entity which may occur to relatively young patients with history of TC within the first 5 years of follow up. ART is generally successful and improves symptoms in the majority of patients.

Histology		
Total	88	
Pure seminoma	57	
NSGCT	22	
Combined	6	
Leydig	3	
Bilateral orchidectomy or atrophic/non existent testis, 40/88	started ART with 2nd surgery	
Single Orchidectomy (SO), 48/88		
Treatment post SO	Carboplatin AUC7	20
	Surveillance	3
	Other (BEP,TIP,EP)	28
From TC diagnosis to 1st symptom	14.96 mo	
From symptom to 1st T level	1.32 mo	
From TC diagnosis to ART	16.67 mo	
Clinical benefit with ART (SO)	Improved	38
	Lost to FU	2
	No benefit	2
	Stopped	2
	Unsure	4

7113 POSTER DISCUSSION

FGF-mechanism of Resistance to VEGF Receptor Antagonists

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Background: The growth of new blood vessels is regulated at multiple steps by interactions between several pro- and antiangiogenic factors. We believe that the angiogenesis induced by basic fibroblast growth factor (bFGF) is resistant to anti-VEGF/R (vascular endothelial growth factor/receptor) therapy.
Methods: The Corneal Micro Pocket Assay was performed. 70 female C57BL/6 mice (age at start day, 6 weeks) were randomized to 7 arms (10 mice in each group): 1) bFGF; 2) VEGF-A; 3) bFGF negative, VEGF-A negative; 4) bFGF and sunitinib; 5) VEGF-A and sunitinib; 6) bFGF and bevacizumab; 7) VEGF-A and bevacizumab. Doses of bFGF, VEGF-A (R&D Systems), sunitinib (Pfizer), and bevacizumab (Roche) were 200 ng, 400 ng, 10 mg/kg, 50 mg/kg per animal, respectively. Hydron pellets preparation, surgical procedure, and quantification of angiogenesis (angiogenic score) were performed as previously reported (Kenyon BM et al.). Statistical significance was determined by the Student's t test.
Results: There was no neovascularization in bFGF negative, VEGF-A negative group (mean, 0). The effect of 200 ng/pellet of bFGF (mean, 4.2; SEM, 0.05) was compared with that of 400 ng/pellet VEGF-A (mean, 4.08; SEM, 0.09), P = 0.7. In bFGF-induced angiogenesis, sunitinib (mean, 3.9; SEM, 0.1; P = 0.2) and bevacizumab (mean, 4.71; SEM, 0.33; P = 0.85) did not impact on neovascularization in comparison with bFGF positive control. The angiogenic effect of VEGF-A was significantly inhibited by both sunitinib (mean, 0.38; SEM, 0.06; P = 0.001) and bevacizumab (mean, 0.75; SEM, 0.05; P = 0.001) in comparison with VEGF-A positive control. No significant differences between 2 targeted agents in bFGF and VEGF-A models were obtained.
Conclusion: Our recent findings demonstrate that anti-VEGF(R) therapy significantly impacts on VEGF-A-induced angiogenesis and not on bFGF-induced neovascularization. Further studies are needed to assess the role of FGF-pathway in resistance to VEGF(R) therapy.

7114 POSTER DISCUSSION

Appropriateness of Treatment Options for the Management of Patients With Advanced Renal Cell Carcinoma (RCC) Using the Validated Semi Quantitative RAND Corporation/University of California, Los Angeles (RAND/UCLA) Methodology

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Background: Targeted therapies have radically improved the outlook for patients with advanced RCC. A number of factors contribute to treatment choice such as prior treatment and prognostic risk assessment (e.g. MSKCC risk criteria). In order to combine up-to-date clinical evidence with the experience of experts in the field, we have undertaken an update of prior work to include newer treatments and evidence, and add a European perspective.
Methods: The RAND/UCLA method was employed using a panel of 11 EU experts. Cases and treatments were grouped according to clinical patient scenarios. Individual panel members scored the appropriateness and their preferences of several interventions for each case and treatment, 1 (inappropriate) to 9 (most appropriate). This was followed by a panel meeting to reconcile disagreements as per the RAND methodology.
Results: There was excellent concordance among the panel for the appropriateness/inappropriateness of therapies for the majority of different clinical scenarios considered with only 4.2% disagreement. There were however a number of areas where the preferences or opinions of panel members varied ("disagreement"). Two such examples were

- Use of sunitinib or pazopanib in two instances, patients with locally advanced tumour and those with metastatic disease and the primary tumour in-situ, with good surgical risk and no prior systemic therapy but with high risk features (MSKCC criteria)
- Use of temsirolimus in papillary and oncocytic carcinoma

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)

B. Beuselinck[1], A. Karadimou[2], G. Couchy[2], B. Claes[3], D. Lambrechts[3], J. Berkers[4], R. Paridaens[1], P. Schöffski[1], J. Zucman-Rossi[2], S. Oudard[5]. *[1]University Hospitals Leuven Catholic University Leuven, Department of General Medical Oncology, Leuven, Belgium; [2]Université Paris-5 René Descartes, Inserm U674 Génomique Fonctionelle des Tumeurs Solides, Paris, France; [3]Catholic University Leuven, Vesalius Research Centrum, Leuven, Belgium; [4]University Hospitals Leuven Catholic University Leuven, Department of Urology, Leuven, Belgium; [5]Hôpital Européen Georges Pompidou Université Paris-5 René Descartes, Department of Medical Oncology, Paris, France*

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