significantly associated with shorter recurrence-free survival in non muscle-invasive urothelial cell cancers. Claudin-10 protein was not detected in the samples and only scattered expression of claudin-3 and -5 proteins was found in a few tumour cases.
Conclusions: Claudins and Ki-67 might be used as potential markers to differentiate low grade and high grade urothelial cell cancers, thereby they might enhance the accuracy of pathological diagnosis and might add further information to clinical outcome.

7118 POSTER

Expression of Claudins and Their Prognostic Significance in Non-invasive Urothelial Neoplasms of the Human Urinary Bladder

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Background: The members of claudin family are major integral transmembrane protein constituents of tight junctions. Normal and neoplastic tissues can be characterized by unique qualitative and quantitative distribution of claudin subtypes which may be related to clinicopathological features. Differential diagnosis and prognosis of non-muscle invasive tumour entities of urinary bladder epithelium are often challenging.
Objective: To investigate expression profile of claudins in inverted urothelial papillomas (IUP), urothelial papillomas (UP), papillary urothelial neoplasms of low malignant potential (PUNLMP) and intraepithelial (Ta), low grade urothelial cell carcinomas (LG-UCC) in order to reveal potential prognostic and differential diagnostic values of certain claudins.
Patients and Methods: Claudin-1, -2, -4 and -7 protein expressions detected by imunohistochemistry and clinical data were analyzed in 15 IUPs, 20 UPs, 20 PUNLMPs and 20 LG-UCCs.
Results: UPs, PUNLMPs and LG-UCCs showed significantly decreased claudin-1 expression in comparison to IUPs. LG-UCCs expressing claudin-4 over median were associated with significantly shorter recurrence-free survival. PUNLMPs expressing claudin-1 over the median revealed significantly longer recurrence-free survival.
Conclusion: High claudin-1 protein expression might help to differentiate IUP from UPs, PUNLMPs and LG-UCCs. High claudin-4 expression may determine unfavorable clinical course of LG-UCCs, while high claudin-1 expression in PUNLMP was associated with markedly better clinical outcome.

7119 POSTER

NAT1 as a Genetic Predisposing Factor for Urinary Bladder Cancer in Lebanese

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Background: Urinary bladder cancer is the fifth most common cancer in Europe and ranks five in the United States. Historically, the majority of studies investigating bladder cancer focused on oncogenes, tumour suppressor genes, and subsequent cellular events. In the last few years, the role of drug-metabolizing enzymes in bladder cancer has come into focus. Genetic variants of metabolic enzymes are thought to result in critical changes in the metabolism of environmental carcinogens, subsequently altering individual bladder cancer risk. Arylamines, the main carcinogens implicated in bladder cancer, are metabolized by N-Acetyl-Transferases 1 & 2 (NAT1 & NAT2) isoenzymes. The reported NAT1 polymorphism suggests that the NAT1 acetylator genotype may be associated with bladder cancer susceptibility. In Lebanon, the rising incidence of urinary bladder cancer in the past few years is alarming. According to the latest National Cancer Registry report, bladder cancer is currently the second most common malignancy in males (15.1%), almost equal to lung cancer (15.2%). The purpose of this study is to investigate a possible association between NAT1 genotype and bladder cancer risk in a group of Lebanese males.
Materials and Methods: 54 cases and 105 hospital controls were randomly selected for the study from two major medical centers in the city of Beirut. Polymerase Chain Reaction-Restriction-Fragment-Length-Polymorphism (PCR-RFLP) was performed on peripheral blood DNA samples to determine NAT1 genotypes, and an interview-based questionnaire was completed to assess suspected risk factors. The association between bladder cancer and putative risk factors was measured using adjusted odds ratios (ORs) and their 95% confidence intervals (CIs) were derived using a logistic regression analysis. Finally, a gene-environment interaction analysis was applied.
Results: A statistically significant 7 fold increased bladder cancer risk (OR= 7.86, 95% CI: 1.53- 40.39) was observed for individuals carrying at least one NAT1*14A allele. An interaction resulted between occupational exposure to fossil fuel emissions and alleles NAT1*14A and NAT1*10.
Conclusions: Our study provides strong evidence that NAT1*14A allele is a genetic predisposing factor for bladder cancer in Lebanese, and suggests a potential gene-environment interaction. Larger studies are needed to confirm these findings to further investigate the role of NAT1 genotype in bladder cancer etiology.

7120 POSTER

Recurrent Testicular Cancer in a Family With MYH-associated Polyposis

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Background: *MYH*-associated polyposis (MAP) is an autosomal recessive inherited syndrome with similar phenotype to attenuated familial adenomatous polyposis. Biallelic germline mutations in *MYH* predispose individuals to multiple adenoma or polyposis coli. Extraintestinal findings are also noted on occasion; breast, gastric, thyroid and haematological neoplasias as well as sebaceous adenomas and hypertrophy of the retinal pigment epithelium have been described. We report on a family with genetic diagnosis of MAP showing a -previously unreported- recurrent extraintestinal cancer.
Material and Methods: Clinical, pathological and genetic characterization of a family with suspected hereditary colorectal cancer. Lynch syndrome screening analysis was performed by tumour tissue analysis of microsatellite instability (MSI) and immunohistochemical expression (IHQ) of MLH1, MSH2, MSH6 and PMS2 proteins. Germline mutation analysis of the *MYH* gene was performed by sequencing of the entire coding region and the intron-exon boundaries. Co-segregation analysis of the genetic findings in the family was also approached.
Results: The index subject was diagnosed of rectal cancer and multiple adenomatous polyps (n = 8) in right colon at age of 44 yrs. Twelve years before was also diagnosed of testicular embryonal carcinoma. Familial history of cancer revealed a brother diagnosed of testicular embryonal carcinoma at age of 28 yrs and a total of 16 adenomatous polyps at age of 44 yrs. Their father has been diagnosed of few polyps at age of 79 yrs. At least, two different syndromes might be suspected: Lynch syndrome and MAP. The rectal cancer showed normal expression of the proteins analyzed by IHQ, and not MSI was detected. Consequently, Lynch syndrome genetic analysis was disregarded. Therefore, *MYH* gene was tested to confirm the alternative suspicious of MAP and founding two heterozygous variants: [c.317G > A]+[c.1227_1228dup]. Both brothers showed the same genotype, and the genetic analysis of their parents demonstrated that those variants were located *in trans*.
Conclusions: Testicular cancer might be a new extraintestinal manifestation of MAP syndrome. Further analysis to establish the causal relation between *MYH* genetic variants and testicular cancer is underway. A better knowledge of the clinical phenotype of individuals with MAP will make possible the identification and the proper management of mutation carriers in the population at risk.

7121 POSTER

Bladder Preservation a Valid Option for Patients With Muscle Invasive Bladder Cancer − Single Centre Experience

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Introduction: Cystectomy is considered the standard of care for patients with muscle invasive bladder cancer, despite the fact that no randomized studies between cystectomy and radiotherapy or chemoradiotherapy exist (to show superiority of cystectomy). Patients however are often either not fit for cystectomy or do not wish to undergo cystectomy, and hence enter bladder preservation protocols. Here we report our experience in Cyprus with our bladder preservation protocol with all patients treated in the last 10 years.
Methods: 38 consecutive patients with muscle invasive transitional cell cancer were treated with bladder preservation in the last 10 years. Neoadjuvant chemotherapy with 3 cycles of Gemcitabine and Cisplatin, was offered to 20 patients with adequate renal function and performance status. After completion of chemotherapy, there was reassessment with cystoscopy

and radiological imaging, and 19 patients without progressive or persistent muscle invasive disease, were offered concurrent chemoradiation with weekly cisplatin 25 mg/m^2. RT dose 64−66 Gy in 1.8−2.0 Gy per fraction with CT planning. Patients unfit to have either neoadjuvant or concurrent chemotherapy, received radiotherapy alone with the same fractionation. Following completion of their treatment, patients had regular cystoscopies (every 3 months) and regular f-up appointments (3−6 months).
Results: 31 male and 7 female patients, median age 75 years, range 27−86 years old (only 6 patients <70 years old). 4 patients had pelvic nodal disease and 1 patient para-aortic lymphadenopathy; they proceeded to CRT after complete response of the nodal disease to neoadjuvant chemotherapy. On follow up there were 5 local relapses (13%) with 2 salvage cystectomies, 1 pelvic lymphadenopathy relapse (3%), 5 distant metastases (13%), whilst 7 patients died without disease progression (18%).
Mean progression free survival (PFS) from the date of starting treatment was in excess of 4.7 years: 1718 days (95% CI 1138 to 2297 days). Mean overall survival (OS) was in excess of 5.1 years: 1882 days (95% CI 1402 to 2362 days). 5 year Kaplan Meier(KM) PFS for the CRT group was 58% compared to 30% for the RT group, whilst 5 year KM OS for the CRT group was 48% with 34% for the RT group.
Conclusions: In an elderly, predominantly unfit for surgery group of patients, bladder preservation with radiotherapy or chemoradiotherapy resulted in very meaningful control of their disease and mean survival of about 5 years.

7122 POSTER

Secondary Cancer Risk for Stage I Seminoma Patients − a Comparison of Adjuvant Treatment Versus Surveillance

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Background: Post-surgical management of stage I seminoma includes: surveillance with repeated CT-scans and treatment reserved for those who relapse, or adjuvant treatment with either immediate radiation therapy (RT) or carboplatin. The cancer specific survival is close to 100%. Cure without long-term sequelae of treatment is the aim. Our goal is to estimate the risk of radiation-induced secondary cancers (SC) death from for patients undergoing S, adjuvant RT or adjuvant carboplatin (AC).
Materials and Methods: We measured organ doses from CT scans (3 phases each one) of a seminoma patient who was part of the active surveillance strategy and from a man undergoing adjuvant RT 20-Gy and a 30-Gy salvage RT treatment to the para-aortic area using helical Intensity Modulated RT (Tomotherapy®) with accurate delineation of organs at risk and a CTV to PTV expansion of 1 cm. Effective doses to organs in mSv were estimated according to the tissue-weighting factors recommendations of the International Commission on Radiological Protection 103 (Ann ICRP 2007). We estimated SC incidence and mortality for a 10,000 people population based on the excess absolute risk model from the Biological Effects of Ionizing Radiation (BEIR) VII (Health Risk of Exposure to Low Levels of Ionizing Radiation, NCR, The National Academies Press Washington, DC, 2006) assuming a seminoma diagnosis at age 30, a total life expectancy of 80 years.
Results: The nominal risk for a fatal secondary cancers was calculated 1.5% for 15 abdominal CT scans, 14.8% for adjuvant RT (20 Gy para-aortic field) and 22.2% for salvage RT (30 Gy). The calculation assumed that the risk of relapse on surveillance and adjuvant AC was 15% and 4% respectively and that all patients were salvaged at relapse with RT.

	n CT abdomen/Pelvis = secondary cancer %	RT Dose and % receiving treatment = secondary cancer %	Total secondary cancer risk in %
Active surveillance	15 = 1.5%	30 Gy in 15% of pts = 3.3%	4.8
Adjuvant carboplatin	7 = 0.7%	30 Gy in 4% of pts = 0.88%	1.58
Adjuvant radiotherapy	7 = 0.7%	20 Gy in 100% of pts = 14.8%	15.5

Conclusions: These data suggest that: 1) Adjuvant radiotherapy is harmful and should not anymore be regarded as a standard option for seminoma stage I. 2) AC seems to be an option to reduce radiation induced cancers. Limitations: the study does not consider secondary cancers due to chemotherapy with AC (unknown). The use of BEIR VII for risk modeling with higher doses of RT needs to be validated.

7123 POSTER

Patterns of Care for Stage 1 Testicular Cancer in Australia in 2010

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Background: There are now several acceptable management options for early stage testicular cancer with cure rates approaching 100%. There is an international trend to surveillance to minimise treatment-associated morbidity.
The Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP) undertook a survey of clinicians involved in the treatment of testicular cancer to determine the patterns of care in Australia and to explore the number and type of imaging procedures used in surveillance strategies.
Methods: An internet-based survey was sent to all clinician members of ANZUP, as well as membership lists of relevant Australian craft groups. The multiple choice questions asked about the management of strategy for all patients treated over the previous 12 months, preferred management strategies, and surveillance imaging protocols. The survey was approved by the University of Sydney Human Research Ethics Committee.
Results: 53 medical oncologists, 10 radiation oncologists, and 7 urologists documented the patterns of care for 644 patients.
For stage 1 seminoma, surveillance was employed in 33%, radiotherapy in 23%, a single dose of adjuvant carboplatin in 34%, and 2 doses of adjuvant carboplatin in 9%. For stage 1 non-seminoma, surveillance was employed in 60%, adjuvant chemotherapy in 35%, and RPLND in 5%.
Surveillance was the preferred strategy for low-risk non-seminoma in 74%, high-risk non-seminoma in 43%, low-risk seminoma in 53%, and high-risk seminoma in 22%.
The mean [SD] numbers of CXR, CT abdomen, and CT chest used in 5 year surveillance strategies for seminoma and non-seminoma were (9.2 [5.6], 9.4 [3.5], 5.1 [4.0]) and (11.8 [7.3], 10.0 [3.6], 6.2 [4.7]) respectively. For seminoma, 7% of clinicians used >15 CT abdomen and 3% used >15 CT chest. For non-seminoma, 8% used >15 CT abdomen and 5% used >15 CT chest.
Conclusion: Our results demonstrate that there is considerable variation in the management of stage 1 testicular cancer within Australia. The high proportion of seminoma receiving adjuvant chemotherapy is contrary to international trends of increasing surveillance. Surveillance protocols were highly variable. The radiation exposure from CT during imaging for surveillance could increase risk of secondary malignancies, particularly for patients receiving >15 CTs. There is a need to reduce radiation exposure from CT imaging for surveillance through standardised follow-up protocols and alternate imaging modalities.

7124 POSTER

Adjuvant Radiotherapy With or Without Chemotherapy in Patients With Stage III/IV Transitional Cell Carcinoma of the Upper Urinary Tract And/or Positive Resection Margin

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Background: The role of adjuvant radiotherapy still remains undefined in patients with transitional cell carcinoma of the upper urinary tract (UTTCC). To evaluate the role of adjuvant radiotherapy, we reviewed the clinical outcomes of patients with advanced stage III or IV UTTCC.
Materials and Methods: Between January 2007 and December 2010, 17 patients with stage III (n = 13) or IV (n = 4) UTTCC (16 patients with ureter cancer and 1 patient with renal pelvis cancer) were treated with nephroureterectomy and adjuvant radiotherapy with or without chemotherapy. As historic control group, we retrospectively reviewed 46 patients who were treated with nephroureterectomy alone for UTTCC between January 2000 and December 2005. All cases were stage III/IV or positive resection margin. 8 of 17 patients (41%) in adjuvant radiotherapy group had positive resection margin including 1 with grossly positive margin, while 7 of 46 patients (15.2%) in surgery alone group had microscopically positive margin. Adjuvant radiotherapy was delivered to tumour bed and regional lymph nodes with median dose of 50.4 Gy (range