BJUI

BAUS Annual Meeting, 15–18 June 2015

Paper Session

Tuesday 16 June
Paper Session 1
1500–1600 Charter 1
BLADDER CANCER
Chair: Mr David Gillatt & Professor Mark Soloway
Papers 7–12

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Workplace patterns and urothelial bladder cancer phenotype – can occupation increase the risk of developing advanced disease?

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Introduction: Urothelial Bladder cancer (UBC) is a common malignancy that can arise from occupational carcinogen exposure. Recent next generation sequencing studies (TCGA) have shown that muscle invasive UBC comprises distinct sub-sets of tumours. We hypothesized that the proportion of non-invasive and invasive UBC, (and disease specific mortality [DSM]), could vary between occupations where workers maybe exposed to different carcinogens triggering a specific disease phenotype.
Patients: We examined UBC incidence, stage at diagnosis and DSM in 1.7 million men (with 13 717 UBCs) and 1.7 million (with 4282 UBCs) women (follow up of 37 and 43 million person years, respectively) with annotated occupational descriptions. We identified DSM in 3615 (26% out of incident UBCs) males and 1414 (33%) females.
Results: Incidence of 'advanced' tumours was higher than in the comparable population for male seamen (standardized incidence ratio 2.15, 95% confidence interval 1.25–3.44), welders (1.86, 1.12–2.90) and miscellaneous construction workers (1.44, 1.10–1.85), and in female construction workers (2.71, 1.00–5.90), and waiters (2.27, 1.30–3.68). Fewer than expected advanced tumors were observed in male teachers (0.53, 0.30–0.86), military personnel (0.17, 0.00–0.94) and chemical process workers (0.24, 0.05–0.71. Higher than expected DSM rates were seen in male building caretakers (1.39, 1.09–1.76), transport workers (1.27, 1.01–1.59), the economically inactive (1.24, 1.14–1.35) and engine operators (1.23, 1.00–1.49), and in female assistant nurses (1.55, 1.01–2.27) and hairdressers (1.99, 1.03–3.47).
Conclusion: We have identified occupations with different risks for bladder cancer phenotype and for DSM. Further work is needed to identify candidate carcinogens that may account for the observed differences.

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Celecoxib for the treatment of non-muscle invasive bladder cancer (NMIBC): Results of the randomised BOXIT trial (CRUK/07/004)

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Introduction: COX-2 is implicated in development and recurrence of bladder cancer. BOXIT aims to determine if adding celecoxib, a COX-2 selective nonsteroidal anti-inflammatory, to standard therapy improves outcomes for patients with NMIBC at high (HighR) and intermediate risk (IntR) of recurrence.
Patients and Methods: 472 NMIBC patients (346 (73%) HighR; 126 (27%) IntR) from 51 centres were randomised to celecoxib 200 mg b.d. ($n = 236$) or placebo ($n = 236$) for two years in a double-blind phase III trial. 373 (79%) participants were male; mean age: 66.4 yrs; 157 (33%) had previous transitional cell carcinoma (TCC) recurrence in past 2 yrs. All patients had normal ECG and no history of cardiovascular (CV) disease. Primary endpoint is time to TCC recurrence. Secondary endpoints include time to progression, safety and tolerability. Subgroup analysis by risk group was pre-planned.
Results: With median follow-up 39 months, 3-year recurrence free rate (RFR) (95% CI) was celecoxib: 69% (62–75%) vs placebo: 63% (56–69%); hazard ratio (HR): 0.81, 95% CI: 0.59–1.11, log-rank $P = 0.19$. 3-year RFR was celecoxib: 76% (69–82%) vs placebo: 67% (59–74%); HR: 0.71 (0.47–1.07) for HighR patients and 51% (38–63%) vs 51% (36–64%); HR: 1.00 (0.60–1.66) for IntR patients. In HighR patients, 3-year progression rates were celecoxib: 9.7% (6.0–15.6%); placebo: 9.2% (5.6–14.8%). Incidence of CV events was higher on celecoxib than placebo (12 vs 4; absolute difference = 3.4%; $P = 0.04$).
Conclusion: Celecoxib increased CV events and was not associated with a

significant improvement in time to TCC recurrence compared to standard treatment for IntR or HighR NMIBC. Further exploration of observed risk group effects is warranted.

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Real life experience: Recurrence free survival at 3 years is significantly better with Hexvix® PDD-TURBT when compared with Good Quality White Light TURBT (GQ-WLTURBT) in new non muscle invasive bladder cancer (NMIBC) – a prospective controlled study

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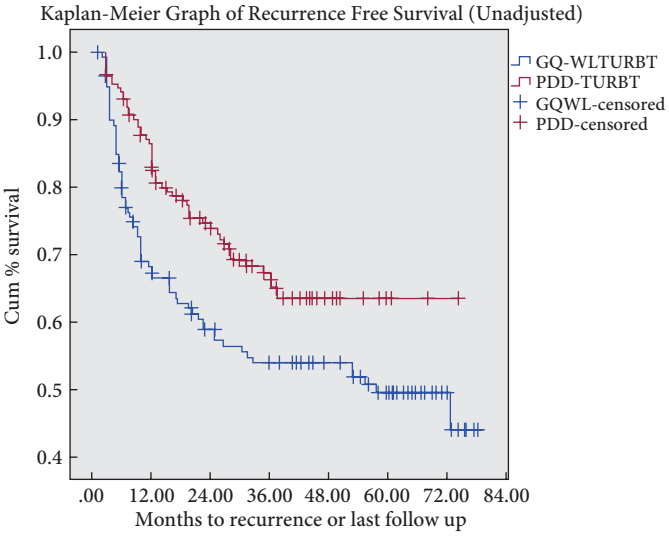
Introduction: We aimed to compare 3 year recurrence rates (RR-3y) between GQ-WLTURBT and PDD-TURBT (using Hexvix®) in a real life controlled setting.
Methods: A prospective controlled study was carried out on consecutive patients with new NMIBC, deemed to have had complete first resections, recruited from a prospectively maintained white light TURBT cohort from 2007–2008 and PDD TURBT cohort from 2009–2011. GQ-WLTURBT was defined by published criteria of TURBT with: (a) cystoscopic mapping using a bladder diagram, (b) documented complete resection of the tumour(s), (c) resection performed or supervised by an experienced surgeon, (d) presence of detrusor muscle in the specimen and (e) patient receiving Mitomycin C within 24-hours of the resection. Recurrence was defined as a biopsy proven tumour. Regression analysis was carried out.
Results: A total of 808 bladder cancer patients were assessed. Median follow up was 55.9 (3.0–78.1) and 35.2 (3.0–80.5) months for the GQ-WLTURBT and PDD-TURBT cohorts, respectively. At a 3 year 'snap-shot', taking into account patient attrition, the actual recurrence was 48.8% following GQ-WLTURBT and 42.2% following PDD-TURBT. Overall ($P = 0.01$, Fig. 1) and risk-group adjusted recurrence free survival (P = 0.003, on Cox regression analysis) was significantly better with PDD-TURBT over GQ-WLTURBT.
Conclusion: Hexvix® PDD assisted TURBT appears to be associated with an improved 3-year recurrence free survival compared with GQ-WLTURBT in this prospective controlled clinical study, representing potential benefits in a real-life setting.

Fig. 1 (Paper 9) Kaplan Meier graph of unajusted recurrence free survival in PDD-TURBT vs GQ-WLTURBT ($P = 0.01$).



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HYMN: a randomised controlled phase III trial comparing hyperthermia plus mitomycin to a second course of BCG or institutional standard in patients with recurrence of non-muscle invasive bladder cancer (NMIBC) following induction or maintenance BCG therapy

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Introduction: The combination of intravesical mitomycin-C with microwave-induced bladder wall hyperthermia (HM) has been proposed as a treatment for post-BCG recurrence in NMIBC. The aim of this trial was to determine whether HM is superior to BCG re-challenge or institutional standard as a salvage intravesical therapy.
Patients and Methods: Patients were randomised 1:1 to receive either HM (experimental arm) or a second course of BCG/institutional standard therapy (control arm). The primary outcomes measures were a) disease-free survival time in all patients and b) complete-response rate at 3 months in patients with CIS at randomisation.
Results: 48 patients were randomised to HM and 56 to the control arm. 71 patients had CIS (49 with CIS alone, 22 with CIS plus papillary disease); 33 patients had Ta or T1, G2/G3 disease with no CIS. The complete response rates at 3 months in CIS patients in the HM and control arms were 81% and 86% respectively. Overall, there was no difference in disease-free survival between the HM and control arms: HR 1.27 (95% CI: 0.77–2.07, $P = 0.34$). However, patients with papillary disease alone ($n = 33$) showed an improved disease-free survival rate in the HM arm: HR 0.40 (95% CI: 0.16–0.98, $P = 0.05$). Conversely, patients with CIS (±papillary disease) ($n = 71$) did not show an improved disease-free survival rate in the HM arm: HR 2.17 (95% CI: 1.15–4.08, $P = 0.02$).
Conclusion: This trial did not show a difference overall between HM and the control arm. However, these data suggest that HM is effective as a second-line therapy in patients with papillary disease alone.

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Oncological outcomes following intracorporeal robotic cystectomy versus open radical cystectomy: an analysis of 184 patients

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Introduction: We compared oncological outcomes of a consecutive series of open (ORC) and intracorporeal robotic assisted (iRARC) cystectomy.
Methods: 184 patients underwent radical cystectomy for transitional cell carcinoma of the bladder. 94 ORC cases and 90 iRARC cases were performed. Primary outcome was recurrence free survival (RFS) measured at 25.3 ± 21.3 months for ORC and 11.1 ± 8.3 months for iRARC (mean ± SD). Secondary outcome was local vs distant recurrence and overall survival.
Results: Multivariate analysis showed no difference in mean age (ORC 66.4 ± 10.6 years, iRARC 64.3 ± 12.3 years), gender, pre-cystectomy T stage, surgical margin status or lymph node yields. There was a higher level of neo-adjuvant chemotherapy (NAC) use in iRARC ($n = 31$; 34.4%) compared to ORC ($n = 23$; 23.0%) and a significant difference in pT0 disease for iRARC ($n = 20$; 22.2%) compared to ORC ($n = 8$; 8.5%) ($P = 0.025$). There was no difference in RFS (66% ORC vs 64% iRARC) or OS (74% ORC vs iRARC 85%) at 24 months. There was a significant difference in RFS of patients with ≥pT2 cystectomy pathology favouring ORC compared with iRARC ($P = 0.002$) (65% vs 36% at 12 months). However, when adjusted for NAC use, tumour stage and grade, there was no significant difference between ORC and iRARC (64% vs 70%) at 24 months. No difference in site of recurrence was observed between ORC and iRARC.
Conclusion: ORC and iRARC have comparable oncological outcomes. In the absence of appropriately designed randomised trails, focus on outcomes for higher stage (≥pT2) disease needs to be adjusted for the increasing use of NAC.

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Robotic radical cystectomy with intracorporeal urinary diversion: Impact on an established enhanced recovery protocol

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Introduction: An enhanced recovery protocol (ERP) after open radical cystectomy (ORC) was introduced in our centre in 2005. A significant change to our service was the introduction of robotic-assisted radical cystectomy (RARC) with intracorporeal reconstruction in 2010.The present study aims to document the outcomes of our ERP over the last decade with particular focus on the impact of RARC with intracorporeal reconstruction.
Methods and Materials: Data on 102 consecutive patients undergoing RARC with full intracorporeal reconstruction was obtained from our prospectively updated institutional database. This data was compared to previously published data from our institution on 168 patients undergoing ORC. Our primary focus was peri-operative outcomes including transfusion rate, complication rates, 30 d and 90 d mortality rates and hospital stay.
Results: The demographics of the two groups showed no significant difference in age, gender distribution, American Society of Anesthesiologists grade (Table 1). A significant reduction in transfusion rate (41% vs 19%) and total complication rate (48% vs 31%) was observed in the RARC vs the open group ($P < 0.001$). The median inpatient stay for the robotic group was 8 days vs 13 days ($P < 0.001$). 30 d and 90 d mortality rates were equivalent between the 2 groups (2%).
Conclusions: Introduction of RARC and intracorporeal reconstruction represents the single biggest impact on our ERP with significant improvements in peri-operative morbidity, transfusion rates and in-patient stay.

Table 1 (Paper 12) Summary of demographics, complication rates and mortality rates.

Variable	Pre-ERP	Post-ERP	Post-ERP II	Robotic
Number of patients	56	56	56	102
Men	42	44	46	71
Women	14	12	10	31
Mean age, years (range)	65.9	65.9	66.4 (37–83)	68.22 (18–86)
Pre-operative radiotherapy	3	2	2	4
Pre-operative chemotherapy	3	2	2	43
ASA				
1	8	9	11	7
2	39	40	40	68
3	9	7	5	27
Transfusion rate, no. (%)	24 (43%)	19 (34%)	23 (41%)	20 (19%)
Overall complication rate, no. (%)	27 (48)	25 (44)	27 (48)	32 (31)
30 day Readmission	6	3	3	3
30 day Mortality	1	1	1	1
90 day Mortality	/	/	/	1

The legends for Figure 1 and Table 1 were amended following initial online publication to reflect the correct abstract numbers.