Drug Development and Cancer Research

Chair: G Wharfe and R Delgoda

(O – 01)

The efficacy of premarin *versus* ketoconazole prostate-specific antigen responses in castrate-resistant prostate cancer in Jamaica

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Objectives: Premarin and ketoconazole are affordable secondary hormonal options available for castrate-resistant prostate cancer (CRPC) in Jamaica. The aim of this study was to compare the relative efficacy of both drugs to decrease prostate-specific antigen (PSA) in CRPC in a population of patients predominantly of African-descent.
Methods: This study retrospectively identified patients with CRPC that presented to the University Hospital of the West Indies and a private urology clinic between the months of January and May 2015. The primary endpoint was to identify the proportion of patients with a decline of ≥ 50% in PSA level after treatment. The relative efficacy was assessed by the time to progression (TTP), an increase in PSA of 25% above nadir with PSA progression defined by Prostate Cancer Clinical Trials Working Group 2 criteria.
Results: Thirty-five patients diagnosed with CRPC were identified; 32 initially treated with premarin and three with ketoconazole. Nine of the patients initially on premarin were crossed over to the ketoconazole treatment group to give twelve patients treated with ketoconazole. Prostate-specific antigen decline of ≥ 50% was observed in 43.8% (14 of 32) and 25% (3 of 12) of patients on premarin and ketoconazole, respectively. The median (95% CI) TTP for patients treated with premarin was 24.00 (19.28–28.724) months and ketoconazole was 13.54 (1.66–25.41) months with no statistically significant difference between the groups ($p = 0.107$; log rank test).
Conclusion: The study did not identify differences in the relative efficacy between premarin and ketoconazole in treating CRPC patients, which may be as a result of the small sample size.

(O – 02)

A potential role for the antidiabetic drug metformin in the treatment of platinum-resistant ovarian cancer

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Objective: The treatment of ovarian cancer is complicated by high drug resistance often linked to over-expression of focal adhesion kinase (FAK). Additionally, cancer cells preferentially metabolize glucose, and hyperglycaemia is considered a promotor of tumour growth. In this context, the antidiabetic drug metformin is now being investigated as a potential treatment. The present study assessed the cytotoxic effects of metformin and FAK inhibitor, PF-573228, as therapeutic adjuncts with carboplatin in the treatment of platinum resistant OVCAR3 ovarian cancer cells.
Method: OVCAR-3 cells were maintained in EMEM complete media (80% EMEM; 20% FBS; 1% antibiotic) with a culture environment of 5% CO_2 and 37 °C. Cells were exposed to metformin (5 mM, 25 mM, 50 mM), carboplatin (1μM,10 μM, 100 μM) and FAK inhibitor PF-573228 (5 μM, 50 μM, 100 μM) over a 24-hour period in triplicates to determine IC_{50}. Twenty- four hour combination treatments of metformin+carboplatin, metformin+PF-573228 and metformin+carboplatin+PF-573228 were carried out in triplicates. Cytotoxicity tests were performed using the MTT assay and absorbance was measured by a spectrophotometer at 570 nm.
Results: Metformin, carboplatin and FAK inhibitor (PF-573228) alone induced a dose-dependent cytotoxicity in OVCAR-3 cells with IC_{50} of 26.31 mM, 57 μM and 100 μM, respectively. For combination treatments, metformin significantly enhanced the cytotoxic effects of carboplatin by 10% ($p = 0.0002$) and PF-573228 by 36% ($p < 0.00001$). The combination result of all three revealed 94% ($p < 0.000001$) cytotoxicity which was significantly higher than metformin only (29%; $p < 0.05$) or carboplatin and PF573228 only which produced 50% cytotoxicity.
Conclusion: Metformin potentiates the cytotoxic effects of carboplatin and PF-573228 in platinum-resistant ovarian cancer cells.

(O – 03)

The outcome of atypical small acinar proliferation at the University Hospital of the West Indies

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Introduction: Prostate adenocarcinoma is the leading male cancer in Jamaica and the leading cause of cancer-related deaths. Atypical small acinar proliferation (ASAP), a histological diagnosis that does not demonstrate all the features of adenocarcinoma, is considered pre-malignant and warrants a repeat prostate biopsy. This cancer is seen in 0.4–23.4% of prostate biopsies and results in an ultimate diagnosis of cancer in 40% of biopsies repeated. We sought to determine the prevalence of ASAP in prostate biopsies done at the University Hospital of the West Indies (UHWI) and determine the outcome of these patients.
Methods: A retrospective analysis of all prostate biopsies performed at the UHWI from January 2000 to December 2007 was done. All histology reports were reviewed and reports confirming ASAP were noted. Medical records of all patients with histology confirming ASAP were reviewed. Outcome of patients including prostate cancer diagnosed and survival were determined. The results were analysed using Stata version 12.
Results: A total of 1670 prostate biopsies were done from January 2000 to December 2007, with 57 (3.4%) having a diagnosis of ASAP. Thirty-two patient records were available for analysis. The mean patient age was 69.2 years. Twenty-five patients had follow-up for repeat biopsies with a cancer detection rate of 31%. Most cancers detected were well to moderately differentiated adenocarcinoma.
Conclusion: The prevalence of ASAP in Jamaica is similar to internationally quoted studies. Close follow-up is required as it is a pre-malignant lesion which may lead to clinically significant prostate cancer.

(O – 04)

The prevalence of use of natural products among prostate cancer patients in Jamaica: a cross-sectional study

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Objective: To determine the prevalence and types of natural products used among prostate cancer patients in Jamaica and whether use predated or followed the diagnosis of prostate cancer.
Methods: This was a cross-sectional study in which patients with prostate cancer, forty years and older, were interviewed and information collected on demographic data, disease stage, and the timing and type of natural products used. The data were analysed to determine if there were associations between demographic variables, stage of disease and natural product use. The study was conducted in the urology clinic of the University Hospital of the West Indies, Jamaica.
Results: Of the patients recruited (200), 56.3% (95% confidence interval [95% CI]: 49, 63.2) were currently taking natural products, whilst 61.6 % (95% CI: 51, 71.9) of those not taking natural products were willing to try them as treatment. The majority of the patients (71%) started taking natural products therapeutically. Guinea hen weed was the most commonly used natural product (89.5%). No statistically significant association between the age of the patients and their willingness to try natural products was found ($p = 0.096$), nor was there any association between the stage of the disease and natural product use ($p = 0.545$).
Conclusion: The majority of Jamaican patients with prostate cancer are currently taking natural products or are willing to take them if they are not already doing so.

(O – 05)

Awareness of the relationship between cigarette smoking and bladder cancer among Jamaicans: a cross-sectional study

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Background: Bladder cancer is the second commonest cancer affecting the urinary tract. Cigarette smoking is the most important population risk factor for bladder cancer but the level of awareness of this risk relationship among Jamaicans is unknown. Determining the level of awareness is important in informing health education programmes aimed at decreasing the incidence of tobacco-related cancers.
Methods: Patients attending the urology clinics at the University Hospital of the West Indies, Kingston, Jamaica, were surveyed utilizing a self-administered questionnaire which enquired about their sociodemographic characteristics and smoking history as well as their opinion regarding a number of risk factors (age, family history, low fibre diet, high fat diet, lack of physical activity, multiple sexual partners and cigarette smoking) in relation to common cancers including lung and bladder cancer. The proportion of patients who were aware of the risk relationship between cigarette smoking and bladder cancer was compared with the proportion aware of the risk relationship between ciga-

rette smoking and lung cancer using the Fisher's exact test. **Results:** One hundred and fifteen patients completed the questionnaire, 57% (65) men and 43% (50) women. The average age of participants was 54 ± 16 years but men (58 years) were on average eight years older than the women (50 years). The majority of the participants was either married or single and had received primary or secondary education. Only 32.4% (36 of 111) (95% confidence interval [95% CI]: 23.9, 42) of persons were aware that cigarette smoking was a risk factor for bladder cancer compared to 93% (106 of 114; 95% CI: 86.6, 96.9) who were aware that cigarette smoking is a risk factor for lung cancer. This difference in awareness was highly statistically significant ($p = 0.0001$). Eighty per cent (4 of 5) of current smokers compared to 28.4% (29 of 103) of non-smokers (Fisher's exact test, $p = 0.031$) were aware of the association between cigarette smoking and bladder cancer.

Conclusions: Knowledge of the awareness of cigarette smoking as a cause of bladder cancer is very poor. Health education efforts should focus on increasing knowledge of the risks of tobacco smoke in causing other cancers including bladder cancer.