Results: Differences between benign prostatic hyperplasia and prostatic carcinomas was observed in high level of expression of PKC isoforms alpha, and delta ($p < 0.001$). PKC isoforms alpha, and delta were elevated in prostate cancer (97%) and in poorly differentiated carcinomas (80%) and reduced to well differentiated prostatic carcinomas and prostate hiperplasia. The frequency of elevated PKC isoforms alpha, and delta expression was higher in tumours with Gleason score >5 ($p < 0.001$).
Conclusions: These results indicate that both PKC alpha and PKC 98delta may aid in prominence between benign and malignant prostatic diseases.

883 POSTER

Phase I trial of sorafenib (BAY 43–9006) in combination with interferon alpha-2a in patients with unresectable and/or metastatic renal cell carcinoma and malignant melanoma

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Background: Sorafenib (BAY 43–9006) is a novel, oral multi-kinase inhibitor that acts on both the tumour and the vasculature by targeting Raf kinase and the receptor tyrosine kinases VEGFR-2 and PDGFR-β. In Phase II/III trials, sorafenib significantly prolonged progression-free survival versus placebo, and had a favourable safety profile in patients with renal cell carcinoma (RCC). This Phase I, single-centre, open-label study was designed to determine the safety profile and maximum tolerated dose (MTD) of sorafenib in combination with interferon alpha-2a (IFN).
Patients and methods: Patients with metastatic RCC or malignant melanoma who were refractory to standard therapy were enrolled. Following a 2-week period of IFN alone, patients received 28-day cycles of continuous oral sorafenib 200 mg (cohort 1) or 400 mg bid (cohorts 2 and 3), with subcutaneous IFN 6 MIU (cohorts 1 and 2) or 9 MIU tiw (cohort 3). Patients continued on treatment until disease progression, unacceptable toxicity or death. Primary endpoints were the safety profile and MTD of combination therapy. Secondary endpoints included RECIST-evaluated best tumour response, changes in tumour vascularization by Doppler US, and various immunological parameters.
Results: Twelve patients with RCC and one patient with melanoma received treatment in cohorts 1 ($n = 4$), 2 ($n = 3$) and 3 ($n = 6$). Patients' characteristics were: median age 59 years (range 25–76); ECOG 0:1, 77%:23%; prior systemic anticancer therapy, 92%; prior IFN, 69%; $\geqslant 3$ metastatic sites, 92%. To date, no dose-limiting toxicities have been reported for patients in any cohort. Common grade 1 and 2 drug-related adverse events occurring in 10 evaluable patients during combination treatment were: fatigue (90% of patients); diarrhoea (80%); nausea (50%); dry skin, hand–foot skin reaction, pruritus and anorexia (40% each). One patient in cohort 2 experienced drug-related grade 3 asthenia; however, this decreased to grade 2 in Cycle 2. One patient in cohort 1 withdrew on Day 6 of Cycle 1 due to grade 2 asthenia and anorexia. No deaths have been reported. Of the nine evaluable patients, stable disease was achieved in five RCC and one melanoma patient, with tumour shrinkage in 5/6 clear-cell RCC patients.
Conclusions: This combination was safe and well tolerated. The recommended dose for Phase II trials is continuous oral sorafenib 400 mg bid and IFN 9 MIU tiw. Complete data will be updated at the meeting.

884 POSTER

The role of amifostine on late normal tissue damage induced by pelvic radiotherapy with concomitant gemcitabine: in vitro study

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Background: In this invitro study; we aimed to assay the role of radioprotective effect of amifostine on late normal tissue damage induced by pelvic radiotherapy with concomitant gemcitabine, by histopatologic and quantitative methods.
Material and methods: Fifty-six male Wistar albino rats were randomly divided into seven experimental groups (8 rats per group) (I) gemcitabine (25 mg/kg) alone (GM) (II) radiation+gemcitabine (25 mg/kg) (RT+GM) (III) radiation+gemcitabine (25 mg/kg)+amifostine (200 mg/kg) (RT+GM+AF) (IV) radiation+amifostine (200 mg/kg) (RT+AF) (V) sham radiation (S) (VI) amifostine (200 mg/kg) alone (AF) (VII) radiation alone (GM). Irradiation was given to the pelvic region with a dose of 20 Gy/5 fractions/5 days with Co60 gamma rays. A single dose of AF (200 mg/kg) was given intraperitoneally 30 minutes before the first day of irradiation. A single dose of GM (25 mg/kg) was injected intraperitoneally 24 hr before the first day of the radiotherapy. TGF-beta levels in plasma were assessed before the beginning of the treatment and 1 week after the treatment. All animals were sacrificed at the end of 4th month. Pathological examination was performed and the tissue collagen content was measured for bladder and rectal tissues.
Results: 52 animals that were alive at the end of the follow up period were analyzed. 35 animals (68.6%) revealed grade I-III late effect in histopathological examination and 5 of them were severe. We observed grade III colitis in 1, bladder fibrosis in 4 animals. In histopathological evaluation, bladder fibrosis and colitis was seen significantly higher in RT+GM groups than the other groups respectively ($p = 0.0027$, $p = 0.0005$). In groups that AF was used, collagen content of bladder and rectal tissue was lower than the other groups ($p = 0.02$ and $p = 0.04$). Although, the collagen contents of bladder and rectal tissues were lower in RT+GM+AF group than RT+GM group, this difference was not significant. The difference between pre-RT and post-RT levels of TGF-B1 was not significant in all groups.
Conclusion: By histopathological and quantitative methods we determined that, addition of amifostine to the pelvic radiotherapy with concomitant gemcitabine can reduce the late bladder and rectal damage. We couldn't show the relationship between plasma TGF-B levels and histopathological radiation injury in pelvic tissues.

Publication
Genitourinary cancer

885 PUBLICATION

Selective organ preservation in muscle-invasive TCC of the bladder: a biological approach

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Introduction: 1400 new cases of T2/T3 TCC bladder are diagnosed in the UK annually. Cystectomy alone is associated with 20–30% local failure rate and raises QoL issues, as reconstruction may not be available/ possible. Neo-adjuvant chemotherapy (neo-CT) has a 5% 5 year absolute survival benefit. (ABC Meta-analysis Collaboration 2003 Lancet;361:1927–34) and pathological response to treatment is associated with outcome (Splinter et al. 1992 J Urol;147:606–8). A pilot study of selective bladder preservation, giving radiation to patients with pathological down-staging after neo-CT is discussed.
Materials and Methods: Patients with T2/T3 TCC bladder received 3 cycles of neo-CT (accelerated MVAC) followed by rigid cystoscopy 2 weeks later. Patients down-staged to $\leqslant$pT1 received radical radiotherapy (64 Gy/32 fractions). Cystectomy was reserved for poor pathological responders ($\geqslant$pT2). Response and toxicity were evaluated.
Results: 24 patients were treated (2000–2004). pCR were seen in 12/25 patients (48%), and pTa/pT1 in a further 7/25 (28%). 21 (88%) patients underwent bladder preservation. After a median of 18 months follow up (8–34) 6 patients have died (metastatic bladder cancer 2, other causes 4) and 1 has required salvage cystectomy for invasive recurrence. 16 (67%) are alive in remission (3 after treatment for superficial disease). Of surviving patients; 15(83%) are alive with an intact bladder. Toxicity has been low with episode of grade 4 bowel toxicity reported.
Conclusion: Selective bladder preservation in patients with favourable pathological response to neo-CT represents a realistic option to cystectomy and merits further evaluation in a multi-centre study.

886 PUBLICATION

Impact of post-implant evaluation by different slice intervals using CT-based dosimetry in prostate brachytherapy

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Purpose: To compare the CT-based post-implant dosimetry by 1 mm slice intervals versus 5 mm slice intervals.
Material and Method: Twenty-one patients treated with permanent prostate brachytherapy were selected for this study.
The CT volume was based on each slice intervals calculated from the contours of the prostate on day 0. One radiologist randomly repeated the contouring and evaluation three times for each slice interval at weekly intervals. Post-implant dosimetry was performed and the DVH were calculated to report the reconstructed prostate volume (pvol), prostate