prostate cancer who had undergone, or were planed for curative intended radiotherapy between December 2006 and March 2010. The QLQ-INFO25 consists of questions regarding the level of perceived information about the disease (4 items), medical tests (3 items), treatment (6 items) and other services (4 items) and 8 single items (different places of care, things you can do to help yourself get well, written information, information on CD tape/video, satisfaction with received information, wish for more or less information and if the information overall had been helpful). For 21 items the response format was a four-point scale from 1 ("Not at all") to 4 ("Very much") and for 4 items "Yes" or "No". Item scores were transformed to a 0 to 100 scale. Higher scores represent higher level of information received, higher information wishes and higher satisfaction.
**Results:** A total of 601 (91%) patients responded to the INFO-25 questionnaire. The mean value and standard deviation (SD) for perceived information about the disease was 55.0 (22.6). Corresponding figures for perceived information on medical tests and treatment were 70.1 (23.6) and 64.6 (21.9). Most patients, 69% were satisfied with the information (42% "quite a bit" and 27% "very much"). Analysis is ongoing and data will be presented on associations between levels of perceived information, information needs, satisfaction with information and time since treatment.
**Conclusion:** Most patients were satisfied with the information, although lack of information concerning information about the disease, medical tests and treatment were observed.

**7063** POSTER

**Bone Scan is of Doubtful Value as a First Staging Test in Prostate Cancer**

L. Carmona[1], G.H. Muir[1], L. Drudge-Coates[1]. [1]*King's College Hospital NHS Trust, Urology, London, United Kingdom*

**Background:** Although reported as having lower sensitivity and specificity than MRI scanning, nuclear bone scanning is still the commonest initial staging test for patients with newly diagnosed prostate cancer. With the hypothesis that primary bone metastases are always in the pelvis or lumbar spine, we wished to assess if bone scan could be replaced by axial imaging as the primary staging test in newly diagnosed prostate cancer (CaP).
**Materials and Methods:** We reviewed all bone scans (n = 1201) identified as being carried out in newly diagnosed prostate cancer patients from 2000 to 2010. Patient age, ethnicity, PSA at diagnosis of CaP, TNM stage, Gleason score and serum Alkaline Phosphatase were recorded for multivariate analysis. The mean age was 72 years (41−96). 57% were white and 38% black. PSA mean PSA was 268.95 (0.5–106931). Gleason 7 was the most common reported (39.38%), followed by Gleason 6 (22%). Mean Alkaline phosphatase was 166 (7–2755). Patients were assigned to one of four groups according to possible bony metastases.
**Results:** See the table.

Results of initial analysis by possible bone metastases diagnosed by bone scan

| | | | |
|---|---|---|---|
| Group 1 | No metastases | 818 | 68.11% |
| Group 2 | Metastases only in pelvis and/or lumbar spine | 136 | 11.32% |
| Group 3 | Widespread metastasis including pelvis and lumbar spine | 223 | 18.57% |
| Group 4 | Distant metastases without pelvic or lumbar spine abnormalities | 24 | 2% |

The 24 patients in group 4 were analyzed in detail: 15 were shown by other imaging to be false positives, 6 were found to have had prior hormone therapy, 1 was diagnosed with multiple myeloma, and another had Paget's disease. Only one had disease that was detected only outside the pelvic and lumbar spine (4% of this group but 0.08% of the total), unfortunately there were not enough images to decide.
**Conclusions:** Bone scan is a useful investigation to confirm and monitor metastasic prostate cancer. However this data suggests that axial imaging is a more appropriate primary staging study, and that bone scan is unnecessary if CT or MRI of the pelvis and abdomen are clear of metastases.

## *Oral Presentations* (Sat, 24 Sep, 11:15−12:30)
## Genitourinary Malignancies − Prostate and Other

**7100** ORAL

**Prostate-specific Antigen and Long-term Prediction of Prostate Cancer Incidence and Mortality in the General Population**

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**Background:** It is largely unknown whether prostate-specific antigen predicts long-term risk of prostate cancer incidence and mortality in the general population. We tested the hypothesis that baseline prostate-specific antigen levels predict long-term risk of prostate cancer incidence and mortality.
**Materials and Methods:** Using a prospective study, we examined 4383 20−94 year old men from the Danish general population followed in the Copenhagen City Heart Study from 1981 through 2009. We measured baseline prostate specific antigen and assessed prostate cancer incidence and mortality as a function of prostate specific antigen using Kaplan–Meier plots of cumulative incidence and Cox proportional hazard models, adjusted for potential confounders.
**Results:** During 28 years of follow-up, 170 men developed prostate cancer and 94 died from prostate cancer. For prostate cancer incidence, the age-adjusted hazard ratio was 2.5 (95% confidence interval 1.6−3.9) for a prostate-specific antigen level of 1.01–2.00 ng/ml, 5.0 (3.1−8.2) for 2.01–3.00 ng/ml, 6.1 (3.2−11) for 3.01–4.00 ng/ml, 12 (7.7−19) for 4.01–10.00 ng/ml, and 44 (26−74) for >10.00 ng/ml versus 0.01–1.00 ng/ml. For prostate cancer mortality, corresponding hazard ratios were 1.8 (1.0−3.1), 3.3 (1.8−6.0), 3.8 (1.6−9.1), 4.7 (2.4−9.2), and 12 (5.0–26.0). For men with prostate-specific antigen levels of 4.01–10.00 ng/ml, absolute 10-year risk of prostate cancer was 11% for age <50 years, 19% for 50−60 years, 21% for 60−70 years, 22% for age >70 years; corresponding values for levels >10.00 ng/ml were 37%, 68%, 73%, and 79%, respectively.
**Conclusions:** Stepwise increases in prostate-specific antigen predicted a 3−44 fold increased risk of prostate cancer and a 2−12 fold increased risk of prostate cancer mortality. Also, absolute 10-year risk of prostate cancer was 11−22% in those with prostate-specific antigen levels of 4.01–10.00 ng/ml and 37−79% in those with levels >10.00 ng/ml. These results may be useful during revisions of guidelines on use of prostate-specific antigen testing in healthy men.

**7101** ORAL

**Variations in Androgen Dependent Clinical Progression Kinetics in Locally Advanced Prostate Cancer**

J. Denham[1], A. Steigler[1], D.S. Lamb[2], D.J. Joseph[3], J. Matthews[4], C. Atkinson[5], N.A. Spry[3], C. D'Este[6]. [1]*University of Newcastle, School of Medicine and Public Health, Newcastle NSW, Australia;* [2]*University of Otago, Wellington Cancer Centre, Wellington, New Zealand;* [3]*Sir Charles Gairdner Hospital, Radiation Oncology, Perth WA, Australia;* [4]*Auckland Hospital, Radiation Oncology, Auckland, New Zealand;* [5]*St Georges Cancer Care Centre, Radiation Oncology, Christchurch, New Zealand;* [6]*University of Newcastle, Centre for Clinical Epidemiology and Biostatistics, Newcastle NSW, Australia*

Trial Name: TROG 96.01: Short-term neoadjuvant androgen deprivation (NADT) and radiotherapy (RT) for locally advanced prostate cancer (PC). Registration No: Australian New Zealand Clinical Trials Registry AC-TRN12607000237482. Status: Closed 31 August 2010 after minimum 10 years follow-up. Sponsors: Australian Government National Health and Medical Research Council; Hunter Medical Research Institute (Newcastle, Australia); AstraZeneca Pty Ltd (Sydney, Australia); Schering-Plough Pty Ltd (Sydney, Australia).
**Design:** Phase III randomised clinical trial.
**Objective:** To determine whether 3 or 6 months NADT reduces mortality after RT.
**Endpoints:** Clinical progression, mortality.
**Background to the present study:** To understand the impact of short term NADT on distant progression after RT for locally advanced PC.
**Methods:** Between 1996 and 2000, 802 eligible men with T2b, T2c, T3, and T4 N0 M0 prostate cancers were randomly allocated radiotherapy alone to 66 Gy (RT), 3 months NADT or 6 months NADT before RT. NADT comprised of goserelin 3.6 mgs monthly sc and flutamide 250 mgs tds orally. Cumulative incidences and interval hazards of local and distant progression were derived and compared across trial arms. Competing risks

models using the Fine and Gray method were adjusted for age, tumour stage, Gleason score and initial PSA.
**Results:** Distant progression was not significantly reduced by 3 months NADT [HR = 0.89, 95% CI 0.60–1.31; p = 0.55] but was reduced by 6 months NADT [HR = 0.49, 0.31–0.76; p = 0.001]. Interval hazards revealed the presence of two distinct waves of distant progression in men receiving RT alone. The first wave occurred within 7.5 years of randomization. The magnitude of the first wave was not reduced significantly in men receiving 6 months NADT with Gleason scores 8−10 [HR = 0.68, 0.30–1.53; p = 0.35], or those experiencing distant progression as a first competing clinical progression [HR = 0.66, 0.41–1.09; p = 0.11]. In contrast the second wave of distant progressions, which occurred 7.5 or more years after randomisation and usually in men with Gleason scores <8, T stage 2 primaries, was halved by 3 months NADT and almost completely prevented by 6 months NADT.
**Conclusions:** Variations in androgen dependent distant progression exist in locally advanced PC that have important implications for successful therapy.

**7102** ORAL

**Association of Benign Prostate Hyperplasia With Prostate Cancer Incidence and Mortality − a Nationwide Cohort Study**

D.D. Orsted[1], S.E. Bojesen[1], S.F. Nielsen[1], B.G. Nordestgaard[1].
*[1]Copenhagen University Hospital Herlev, Clinical Biochemistry, Copenhagen, Denmark*

**Background:** Although benign prostate hyperplasia and prostate cancer share features such as hormonal dependent growth and response to treatment with anti-androgen therapy, benign prostate hyperplasia is generally not considered a pre-malignant lesion. We tested the hypothesis that clinical benign prostate hyperplasia associates with increased risk of prostate cancer incidence and mortality.
**Materials and Methods:** Using a prospective design with individual participant data from five national registries, we studied 3,009,258 Danish men. We collected prostate cancer diagnoses (n = 53,315), information on prostate cancer mortality (n = 25,459) and ascertained clinical benign prostate hyperplasia through hospitalization (n = 187,591) and/or operation (n = 77,698) in 1980–2006 and use of $\alpha$-adrenergic receptor antagonists (n = 143,365) and/or use of 5-$\alpha$-reductase inhibitors (n = 47,465) in 1995–2006.
Prostate cancer was assessed by status of benign prostate hyperplasia using Kaplan–Meier plots of cumulative incidence and Cox proportional hazard ratios, adjusted for potential cofounders, with men without benign prostate hyperplasia as reference group.
**Results:** For entire cohort studies, multivariate-adjusted hazard ratios for prostate cancer incidence were 2.22 (95% confidence interval 2.13 to 2.31) in men hospitalized and 3.26 (3.03 to 3.50) in men operated for benign prostate hyperplasia, versus general population controls. Corresponding hazard ratios for prostate cancer mortality were 2.00 (1.91 to 2.08) for hospitalization and 7.85 (7.40 to 8.32) for operation. For age-matched cohort studies, corresponding hazard ratios for prostate cancer incidence were 3.04 (2.96 to 3.13) for hospitalization, 2.60 (2.47 to 2.73) for operation, 4.49 (4.33 to 4.65) for $\alpha$-adrenergic receptor antagonist use, and 2.54 (2.40 to 2.68) for 5-$\alpha$-reductase inhibitor use.
**Conclusion:** In Danish men followed for up to 27 years, clinical benign prostate hyperplasia associated with a 2−3 fold increased risk of prostate cancer incidence, and with a 2−8 fold increased risk of prostate cancer mortality.

**7103** ORAL

**Association of Single Nucleotide Polymorphisms (SNPs) in VEGF Pathway Genes With Progression-free Survival (PFS) and Blood Pressure (BP) in Metastatic Renal Cell Carcinoma (mRCC) in the Phase 3 Trial of Axitinib Versus Sorafenib (AXIS Trial)**

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**Background:** In the randomized, open-label, phase 3 AXIS trial in second-line mRCC (clinicaltrials.gov NCT00678392), axitinib demonstrated a statistically significant improvement in PFS compared to sorafenib (median 6.7 *v* 4.7 months; hazard ratio 0.665, $P < 0.0001$). This study also explored potential associations between germline SNPs in VEGF pathway and genes with PFS and BP-related endpoints.
**Material and Methods:** DNA samples (n = 263, 36% of patients) from blood were genotyped using Taqman allelic discrimination. Potential associations between SNPs in VEGF pathway genes (*VEGF-A*, *VEGFR1*, *VEGFR2*, *HIF1*$\alpha$) and PFS were evaluated in the Caucasian subpopulation only (n = 249), as well as between SNPs in *VEGF-A*, *VEGFR1*, and *VEGFR2* with hypertension (Grade 3 or greater) and high BP (at least one diastolic BP [dBP] reading $\geqslant$90 mmHg).
**Results:** Differences in PFS were seen with *VEGF-A* SNPs rs1570360 (adjusted $P = 0.127$; Cox regression interaction test), rs699947 ($P = 0.058$), and rs833061 ($P = 0.058$). Log-rank tests indicated that potential associations between PFS and genotype for these three SNPs are driven more by differences in PFS among genotypes in the axitinib arm than in the sorafenib arm. For example, the median PFS for *VEGF-A* rs699947 A/A in axitinib-treated patients was 52 weeks (versus 28 weeks for other genotypes; adjusted $P = 0.16$), while no difference in PFS among these genotypes was noted in sorafenib-treated patients (adjusted $P = 0.95$). After adjusting for multiple testing, no statistically significant correlations were observed between SNPs and hypertension or high dBP using logistic regression analysis.
**Conclusions:** Three *VEGF-A* SNPs were potentially associated with PFS. None of the VEGF pathway SNPs examined was associated with axitinib-related hypertension or dBP. These results support previously reported associations of rs1570360 and rs699947 with overall survival in a trial of a bevacizumab-based regimen (Schneider et al, JCO 2008;26:4672), and association of germline SNPs with efficacy for pazopanib (Xu et al, ASCO GU 2011:303). These exploratory data suggest that specific SNPs might help to explain some of the observed interpatient variability in PFS for RCC patients receiving axitinib therapy. Moreover, germline SNPs might be important tools in the future to guide selection of VEGF inhibitors.

**7104** ORAL

**Bone Mineral Density Loss and Fractures in the TROG 03.04 (RADAR) Trial**

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**Clinical trial information:** Trial name: TROG 03.04 (RADAR). Australian New Zealand Clinical Trials Registry Number: ACTRN12607000097448
**Objectives:**
1. To improve prostate cancer specific mortality and PSA progression;
2. To reduce or delay the incidence of bone metastases and prevent leuprolide-induced osteopenia.

**Design:** Phase 3 randomised controlled trial.
Trial status: Closed to recruitment; Follow-up phase. Trial sponsors: National Health and Medical Research Council (Australia), Health Research Council (New Zealand), Novartis Pty Ltd (Australia).
**Background:** Prospective bone mineral density (BMD) and fracture data following androgen deprivation (AD) $\pm$ bisphosphonates were endpoints in the RADAR trial for locally advanced prostate cancer (LAPC).
**Methods:** Between 2003 and 2007 1071 men with LAPC were randomly allocated to short-term (6 months) neo-adjuvant AD using leuprolide and radiation (STAD) either alone, or followed by intermediate term (12 months) AD (ITAD), or accompanied by 18 months of zoledronic acid [4 mg- i.v. q 3 mo ] (STADZ), or accompanied by both (ITADZ). Thoraco-lumbar X-rays (TLX) were done on all men before randomisation and 3 years after to document 'silent' fractures, and DEXAs were obtained prior to randomisation, and at 2 and 4 years after in a nested substudy of 200 men. All symptomatic fractures after randomisation were documented too.
**Results:** Loss of BMD at 2 years was significantly greater in men receiving STAD and ITAD without zoledronic acid. Further changes at four years indicated spontaneous recovery in some men, particularly those treated with STAD and continued loss in others. Use of zoledronic acid also reduced silent TLX fractures in multi-variable models of the BMD data ($p < 0.025$) and in men experiencing symptomatic fractures with osteopenic contribution (n = 28) in the entire study population ($p = 0.056$). Updated data and silent fracture TLX data, currently under review, will also be presented.
**Conclusions:** Zoledronic acid reduces BMD loss and fractures due to both STAD and ITAD.