PCN18

AN EPIDEMIOLOGICAL MODEL OF PROSTATE CANCER AND PROGRESSION TO BONE METASTASES IN THE UNITED KINGDOM

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INTRODUCTION: A high proportion of patients with metastatic prostate cancer (mPC) have bone metastases (BM) which are associated with a high level of morbidity, including bone pain and skeletal related events. Although the epidemiology of prostate cancer is well documented in the United Kingdom, data on the stage at diagnosis, survival of metastatic cancer and data on incidence / prevalence of BM subsequent to prostate cancer are surprisingly scarce for such a common disease. **OBJECTIVES:** To develop a disease model to estimate the number of men with BM due to PC in the UK from 2010 to 2020. **METHODS:** A four-stage disease model (non-mPC, mPC, death from PC, death-other causes), simulating the progression of PC was developed to estimate the incidence and prevalence of mPC and BM in the United Kingdom. The incidence-based model was run over 50 years to obtain incidence and prevalence data. A 1-year cycle length was used. Inputs were obtained from published official sources. Validation used UK national statistics on number of cases / deaths with PC. After validation, a BM-component was fitted within the PC model to ensure consistency with the UK national statistics and obtain estimates of the future incidence and prevalence of BM in the United Kingdom. **RESULTS:** The model estimated an increase in new patients with PC from 2006 to 2020 from 35,510 to 47,417. mPC patients will increase from ~20,000 (1990) to 66,100 (2020). Assuming a 30% prevalence of BM and a RR of 1.35 for survival with BM compared to visceral metastases, the number of PC diagnosed men living with BM ranges from 6,000 (1995) to ~16,200 (2020). **CONCLUSIONS:** This disease model shows that the prevalence of PC is expected to increase in the UK. A substantial number of patients with mPC will develop BM though this is expected to be stable.

PCN19

AN EPIDEMIOLOGICAL MODEL OF BREAST CANCER AND PROGRESSION TO BONE METASTASES IN THE UNITED KINGDOM

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INTRODUCTION: Approximately 65-75% of patients with metastatic breast cancer (mBC) suffer from bone metastases (BM). Complications include pain, impaired mobility, hypercalcemia and pathologic fractures, affecting quality of life and prognosis. The epidemiology of breast cancer is well documented. Data on the incidence and prevalence of BM subsequent to breast cancer are scarce. **OBJECTIVES:** To develop a disease model to estimate the number of women with BC and BM due to BC in the United Kingdom from 2010 to 2020. **METHODS:** A four-stage incidence-based disease model (non-mBC, mBC, death from BC, death-other causes), simulating the progression of BC was developed to estimate the incidence and prevalence of mBC and BM in the UK. It was run over 50 years using a 1-year cycle length. Inputs were obtained from published sources. Validation used UK national statistics on number of cases / deaths with BC. After validation, a BM-component was fitted within the BC model to ensure consistency with UK national statistics and to obtain estimates of the future incidence and prevalence of BM from BC in the United Kingdom. **RESULTS:** New cases of BC in the United Kingdom are predicted to reach ~53,500 in 2020. Deaths due to BC are expected to decrease from ~15,750 to ~11,300 deaths in 2020. Cases of mBC will likely remain stable at ~25,500 cases. Assuming a 54% prevalence of BM in mBC, a RR of 1.42 for survival with-BM versus other-BM, the number of women with BM is assumed to remain stable at ~14,000. **CONCLUSIONS:** This model provides new data for BMs in BC. Predictions are in line with expectations from official sources. The model shows that a substantial number of women with BC will develop BM. Because of the large female population living with mBC, a significant opportunity remains to improve outcomes in patients with BM.

PCN20

EXERCISE LOWERS ESTROGEN AND PROGESTERONE LEVELS IN PREMENOPAUSAL WOMEN AT HIGH RISK OF BREAST CANCER

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OBJECTIVES: Experimental and clinical data support a role for estrogens in the development and growth of breast cancer, and lowered estrogen exposure reduces breast cancer recurrence and new diagnoses in high-risk women. There is varied evidence that increased physical activity is associated with breast cancer risk reduction in both pre- and postmenopausal women, perhaps via lowered estrogen levels. The purpose of this study was to assess whether exercise intervention in premenopausal women at increased breast cancer risk reduces estrogen or progesterone levels. **METHODS:** Seven healthy premenopausal women at high risk for breast cancer completed a seven-menstrual-cycle study. The study began with two pre-intervention cycles of baseline measurement of hormone levels via daily first-morning urine collection, allowing calculation of average area-under-the-curve (AUC) hormone exposure across the menstrual cycle. Participants then began 5 cycles of exercise training to maintenance of 300 minutes per week at 80-85% of maximal aerobic capacity. During the last two exercise cycles, urinary estradiol and progesterone levels were again measured daily. **RESULTS:** Total estrogen exposure declined by 18.9% and total progesterone exposure by 23.7%. Declines were mostly due to decreased luteal phase levels, though menstrual cycle and luteal phase lengths were unchanged. **CONCLUSIONS:** The study demonstrated the feasibility of daily urine samples and AUC measurement to assess hormone exposure in experimental studies of the impact of interventions on ovarian hormones. The results suggest value in exercise interventions to reduce hormone levels in high-risk women with few side effects and potential for incremental benefits to surgical or pharmacologic interventions.

PCN21

PATTERNS OF ANGIOGENESIS INHIBITOR TREATMENT IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA (MRCC) IN IRELAND

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OBJECTIVES: This study evaluated rates of treatment modifications and reasons for these changes among patients treated with angiogenesis inhibitors in Irish clinical practice. **METHODS:** Data from medical records were retrospectively reviewed at 3 large oncology centers in Ireland for mRCC patients who were ≥18 years and received sunitinib (N=54), sorafenib (N=9), bevacizumab (N=6), or temsirolimus (N=7) as first-line treatment from January 1, 2005 to August 31, 2010. Proportions of patients with treatment discontinuation, interruption, or dose change, and reasons for modifications and time to modifications were determined. **RESULTS:** Due to small sample sizes in other groups, only results for sunitinib are summarized. Patients totaling 1.9% had prior cytokine therapy. Median first-line angiogenesis inhibitor treatment duration for sunitinib was 8.7 months. A total of 87% of patients treated with first-line sunitinib experienced ≥1 adverse event (AE); 18.5% experienced ≥1 grade 3/4 AE. 70.4% of patients discontinued first-line sunitinib mainly due to progressive disease (38.9%). AEs were the main reason for treatment interruption among 20 (37%) patients that had an interruption. A total of 94.4% of patients started treatment on 50 mg QD 4/2 dosing; 33.3% of them were dose reduced to 37.5 mg QD 4/2 with median time to reduction 2.7 months. Overall, 77.8% of the patients had ≥1 treatment modification. Adverse events led to treatment modifications in 42.6% of patients. Among patients who discontinued treatment, 31.6% discontinued within 18 weeks (15.8% within 0-6 weeks, 7.9% in 7-12 weeks, and 7.9% in 13-18 weeks). Among patients who discontinued treatment within 18 weeks, 66.7% discontinued due to AEs. **CONCLUSIONS:** Over three-quarters of sunitinib patients experienced treatment modifications, more than half due to AEs. About 24% of treatment discontinuations occurred within the first 2 cycles. This real-world practice study suggests that treatment tolerability is a challenge for physicians in the clinical care of mRCC patients.

PCN22

ASSESSMENT OF SAFETY PROFILE OF TRASTUZUMAB IN METASTATIC BREAST CANCER PATIENTS

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OBJECTIVES: Trastuzumab is a recently approved monoclonal antibody for the treatment of HER2 positive women with metastatic breast cancer (MBC). It shows less toxicity than cytotoxic chemotherapy. The objective of this review was to assess the safety profile of trastuzumab monotherapy in the treatment of HER2 positive women with MBC. **METHODS:** A comprehensive search was conducted in the Cochrane Library, EMBASE and PUBMED to identify randomised controlled trials (RCTs) and single-arm studies assessing the safety of trastuzumab, as monotherapy, in adult HER2 positive women with MBC. The searches were conducted from the database start to January 2011. Only English language studies were included. Eligibility of trials was assessed by two blinded reviewers with any discrepancy resolved by a third independent reviewer. Adverse events were the outcome of interest. **RESULTS:** A total of 518 citations were retrieved of which five studies met the inclusion criteria. This constituted a total of 2229 patients. Safety data showed that gastrointestinal adverse effects (6.68%) were most frequent followed by decrease in left ventricular ejection fraction (LVEF) (6.59%), infection (3.86%), pain (3.14%), headache (2.87%), chills (2.33%), congestive heart failure (1.93%), cough (1.84%), fatigue (1.44%), dyspnoea (1.21%) and pyrexia (0.76%). **CONCLUSIONS:** Results show a higher incidence of gastric and cardiac adverse events compared to other adverse events. Long term studies are required to evaluate risks that may be associated with trastuzumab.

PCN23

IMPACT OF US FOOD AND DRUG ADMINISTRATION'S BLACK BOX WARNINGS ON ADVERSE EVENTS REPORTING RATES FOR MULTIPLE MYELOMA DRUGS

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OBJECTIVES: To determine whether the issuance of a new or revised Black Box Warning (BBW) for an Adverse Drug Reaction (ADR) by US Food and Drug Administration (FDA) increases the proportional reporting of the ADR to the FDA's Adverse Event Reporting System (AERS). **METHODS:** We compiled a list of Multiple Myeloma (MM) drugs with BBWs issued after the drug approval: melphalan, thalidomide, vincristine, carmustine, and doxorubicin. We searched the AERS database for MM drugs and ADRs listed in BBWs and retrieved all cases. We calculated the empiric bayes geometric mean (EBGM) values and clinical outcomes (chi-square analyses) for each drug and ADR combination and compared them before and after the issuance of the BBW. **RESULTS:** EBGM signals increased for 8 of 10 BBW drug/events: melphalan/leukemia (12.83 to 15.97); melphalan/chromosomal aberrations (0 to 18.677); melaphalan/bone marrow suppression (5.926 to 7.629); thalidomide/venous thrombosis (1.201 to 2.464); intrathecal vincristine/death