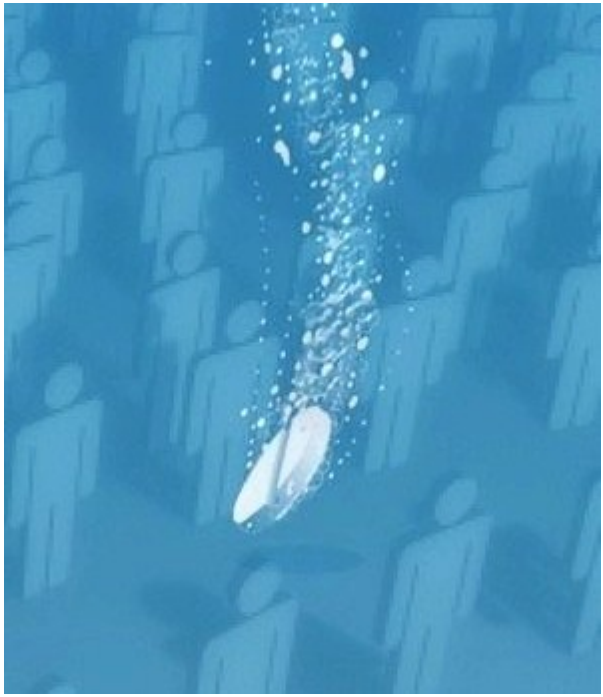
CANCER PHARMACOEPIDEMIOLOGY SYMPOSIUM

23rd September 2013, Dublin



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TRINITY COLLEGE DUBLIN

National Cancer Registry Ireland

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Welcome and Acknowledgment

We are delighted to welcome our visiting speakers, guests and delegates to the Cancer Pharmacoepidemiology Conference in Dublin.

This conference was jointly organised by Trinity College Dublin and the National Cancer Registry Ireland with the generous support of the HRB, who provided funding for the event under the knowledge exchange and dissemination (KEDs) award.

Dr Kathleen Bennett, Trinity College Dublin
Dr Ian Barron, Trinity College Dublin
Dr Linda Sharp, National Cancer Registry Ireland (NCRI)
(Conference Organisers)

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National Cancer Registry Ireland

Morning Programme

9.00	**Registration & Tea/Coffee**		
9.30	**Welcome and opening comments: Dr. Harry Comber, National Cancer Registry Ireland (NCRI)**		
9.40-10.50 **Session 1: Potential for pharmacoepidemiology to inform pre-clinical/molecular studies**			
9.40	How effects of commonly used drugs on cancer incidence/ progression might vary by tumour characteristics	Professor Liam Murray, Queen's University, Belfast	**Chair: Dr Linda Sharp, National Cancer Registry Ireland**
10.15	Aspirin, breast cancer and the future of pharmaco-/molecular epidemiology in Ireland	Dr Ian Barron, Trinity College Dublin	
10.50	**Tea/Coffee & Posters**		
11.10-12.15 **Session 2: Using linked databases for cancer pharmacoepidemiology**			
11.10	The Danish Registry Network & Cancer Pharmacoepidemiologic Research	Dr Deirdre Cronin-Fenton	**Chair: Dr Kathleen Bennett, Trinity College Dublin**
11.45	Cancer and pharmacoepidemiology in Finland - Information sources and research possibilities	Dr Miia Artama, Finnish Cancer Registry	
12.15	**KEYNOTE Speaker**: Dr Kala Visvanathan, John Hopkins University **Comparing traditional epidemiology to registry based cohorts**		
1.00	**Lunch/ Posters**		

Afternoon Programme

2.15-3.00 **Selected abstracts**			
2.15	Beta-blocker usage and colorectal cancer survival: a nested case-control study in the UK Clinical Practice Research Datalink cohort	Blanaid Hicks, Queen's University, Belfast	**Chair: Professor Lonneke van de Poll-Franse, Eindhoven Cancer Registry**
2.30	Association between the use of statins and development of monoclonal gammopathy of un-determined significance and multiple myeloma: a case-control study within CPRD	Charlene McShane, Queen's University, Belfast	
2.45	Low-dose aspirin usage after colorectal cancer diagnosis and survival: A population based cohort study	Andrew Kunzmann, Queen's University, Belfast	
3.00	**Tea/Coffee & Posters**		
3.20-4.30 **Session 3 – Economic & other aspects of cancer pharmacoepidemiology**			
3.20	Use of Drug register data in Swedish Cancer Studies	Professor Mats Lambe & Dr Hans Garmo	**Chair: Dr Lesley Tilson, National Centre for Pharmaco-economics (NCPE)**
3.55	Pharmaco-epidemiological outcome research using the PHARMO Eindhoven Cancer Registry linkage	Professor Lonneke van de Poll-Franse	
4.30	**Close**		

Guest Speaker Biographies

(in order of presentation)

Professor Liam Murray Professor of Cancer Epidemiology, Queen's University Belfast (QUB)

Liam Murray is Professor of Cancer Epidemiology in Queen's University Belfast (QUB). He qualified in Medicine in 1986 and spent 7 years in clinical practice before beginning training in public health and epidemiology in Bristol and Belfast. He leads the QUB Cancer Epidemiology and Health Services Research Group, a multidisciplinary research group within the School of Medicine, Dentistry and Biomedical Science.

Professor Murray has a particular interest in cancers of the gastro-intestinal tract, especially oesophageal adenocarcinoma, and its precursor Barrett's oesophagus. He is PI Northern Ireland Barrett's Register and is a member of the NCI sponsored Barrett's Esophageal Adenocarcinoma Consortium of oesophageal adenocarcinoma and Barrett's studies (BEACON). He also has a major interest in pharmaco-epidemiological studies in the cancer field with a focus on the impact of commonly prescribed medications on cancer incidence and progression.

He has published widely, has over 180 publications in international scientific journals including in JAMA, BMJ, Journal of the National Cancer Institute (JNCI), Gastroenterology etc.

Dr Ian Barron Post-doctoral Research fellow, Trinity College Dublin

Dr Ian Barron, has a PhD in Pharmacoepidemiology, Trinity College Dublin, MSc in Hospital Pharmacy (TCD) and a BSc (Pharmacy) . Dr Barron's primary research interest is cancer pharmacoepidemiology, with a strong focus on studies examining associations between medication exposures and cancer outcomes.

His current research concentrates on the conduct of pharmacoepidemiologic analyses to provide validation or refutation of preclinical study results as part of the translational oncology research pathway. Much of this research is carried out using the linked NCRI-PCRS, cancer and prescribing database. Dr Barron has more than 7 years' experience working with the PCRS prescribing database and has been involved with the NCRI-PCRS database linkage since its inception in 2006.

Dr Deirdre Cronin-Fenton Department of Clinical Epidemiology, Aarhus University Hospital and Institute of Clinical Medicine, Aarhus University

Deirdre Cronin Fenton is an Associate Professor of Breast Cancer Epidemiology at the Department of Clinical Epidemiology, Aarhus University, Denmark. Her research interests primarily lie in cancer epidemiology, specifically cancer risk and prognosis, and how molecular and genetic techniques can be applied to population-based research in order to further understand the risk and prognosis of cancer. She has conducted several studies to date incorporating molecular and genetic epidemiology, pharmacoepidemiology, and pharmaco-genetics. Most of her research has focused on breast cancer treatment, prognosis and etiology, however she is also interested in comorbid diseases and cancer prognosis generally, and biomarkers and cancer.

Dr. Cronin Fenton obtained her B.Sc. in Biomedical Sciences from University College Cork in 1997, and a Ph.D. in Biotechnology (molecular biology and cancer research) from the National Institute for Cellular Biotechnology, Dublin City University in 2002. After her Ph.D. studies, she was awarded a three-year All-Ireland Cancer Consortium Fellowship in Cancer Epidemiology divided between the National Cancer Institute, USA, and the National Cancer Registry of Ireland. Since 2006, Dr. Cronin Fenton has worked as an epidemiologist and Project Director at the Department of Clinical Epidemiology, Aarhus University, Denmark. She has authored approximately 50 papers published in peer-reviewed scientific journals.

Dr Miia Artama Post-doctoral researcher, Finnish Cancer Registry and Center of Excellence in Cancer Genetics

Dr. Miia Artama works as a post-doctoral researcher in the Finnish Cancer Registry and Center of Excellence in Cancer Genetics, funded by Academy of Finland. She has a PhD in epidemiology (2007) and has an expertise in working with Finnish national administrative health registers related to drug use, cancers, pregnancy and birth health (perinatal health, malformations).
Dr. Artama has previous working experience from University of Tampere, University of Helsinki, University of Turku, and National Institute for Health and Welfare, which maintains several national administrative health registers in Finland. She has been working for several years as a research manager with database including Finnish population level information on drug exposures, chronic diseases, and health outcomes. She has conducted several pharmaco-epidemiological case-control and cohort studies based on information obtained from these registers in addition with clinical data.

Dr. Artama is collaborating in several ongoing Nordic, and international pharmacoepidemiological, register-based studies. First results of these studies have been published in high-impact factor scientific journals (Stephansson et al. JAMA. 2013 Jan 2;309(1):48-54, Kieler et al. BMJ. 2012 Jan 12;344:d8012). She has ongoing research collaboration with Columbia University, New York with a 5 years research funding from National Institutes of Health, US. Dr. Artama has been working in European Network of Centres for Pharmacoepidemiology (EnCePP) work groups and plenary meetings in European Medicines Agency since 2008. She is a chairman of the Finnish National Society of Pharmaco-epidemiology.

Dr Kala Visvanathan John Hopkins University , Baltimore, USA

Kala Visvanathan is an Associate Professor in the Department of Epidemiology at Johns Hopkins Bloomberg School of Public Health with a joint appointment in the Department of Medical Oncology at Johns Hopkins School of Medicine. She is both a cancer epidemiologist and a practicing medical oncologist

She received her medical degree from the University of Sydney in Australia. She subsequently went on to complete her training in Internal Medicine and Medical Oncology including a period as Chief Resident at Royal Prince Alfred Hospital, an academic teaching hospital of the University of Sydney in Australia. She also obtained a Masters in Clinical/Cancer epidemiology at the Johns Hopkins Bloomberg School of Public Health and completed further postdoctoral training in medical oncology and epidemiology at Johns Hopkins before joining the faculty in both the School of Public Health and School of Medicine.
Her research is focused on reducing the incidence and mortality from breast and ovarian cancer. Trained as a medical oncologist and cancer epidemiologist, a large part of her research is multidisciplinary and focused on translating results from the laboratory to populations, to identify at risk groups, preventable targets and to evaluate agents that have the potential to impact the natural history of breast and ovarian cancer. Specific exposures of interest include hormonal exposures, inflammation, genetic and epigenetic changes, DNA damage/repair, obesity and oxidative damage. She conducts both observational studies and clinical prevention/early detection studies. Dr. Visvanathan is well published, has obtained peer-reviewed grants, been on a number of study sections and advisory boards. She directs courses both in the Department of Epidemiology and School of Medicine and has served as an advisor to doctoral and masters students as well as clinical fellows, post-docs and junior faculty. She is a co-PI on an HRB ICE award focused on Building future leaders in Population Health and Health Services Research in Ireland. Dr. Visvanathan recently co-chaired the American Society of Clinical Oncology national guideline on breast cancer risk reduction.

Professor Mats Lambe Professor of Medical Epidemiology at the Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Sweden.

Mats Lambe completed his Master's degree in public health at the University of Hawaii 1981, gained a degree in medicine in 1983 from Uppsala University and was awarded a PhD in 1995 for research on cancer epidemiology at the same university. Since 2002 he has been a senior lecturer at the Department of Medical Epidemiology (MEB). From 2003 to 2005 he worked for Astra Zeneca as a senior adviser on cancer epidemiology. From 2007-2011 he was operations manager for the Regional Cancer Centre (RCC) Uppsala Örebro.

Mats Lambe's current research focuses on a quality register of cancers, especially breast, pancreatic and lung cancer, that are linked to the national health data registers held by the National Board of Health and Welfare and SCB databases. He is also the Head of Department for Registers and Care programmes at Regionalt Cancercentrum (RCC) Uppsala Örebro, one of six regional cancer centres in Sweden.

Dr Hans Garmo Regional Cancer Centre, Akademiska Sjukhuset, Uppsala, Sweden; Cancer Epidemiology and Population Health, King's Health Partners Integrated Cancer Centre, King's College, London

In addition to his work at King's College London, Hans also has a part-time affiliation with PCBaSe Sweden, a database based on the National Swedish Prostate Cancer Registry. Hans has been involved in numerous studies using the different Swedish National Health Registers and therefore has extensive experience in complex database management and statistical analyses.

Professor Lonneke van de Poll-Franse Professor of Cancer Epidemiology and Survivorship, Eindhoven Cancer Registry.

Lonneke van de Poll completed her Master's in Epidemiology at the University of Nijmegen in 1995, and obtained her PhD on Diabetes Epidemiology in 2001. Since then she works at the Eindhoven Cancer Registry. Related to the topic of her PhD she became interested in the relation between diabetes and cancer. The linkage between the Eindhoven Cancer Registry and PHARMO (In-and out-patient pharmacy data) is now used by her research group to study this area of interest.

In 2004 she initiated a quality of life pilot study among breast cancer survivors, using the cancer registry as a sampling frame. This was the beginning of a new research activity that laid the foundation of the current PROFILES (Patient Reported Outcomes Following Initial treatment and Long-term Evaluation of Survivorship) registry. Combining PROFILES, the Eindhoven Cancer Registry and PHARMO provides opportunities to evaluate the impact of (new) treatments not only on medical outcomes but also on patient reported outcomes. Together with patients, oncology specialists and researchers from the Comprehensive Cancer Centre South and the Center of Research on Psychology in Somatic diseases (CoRPS) at Tilburg University several large cohorts of cancer survivors are being followed.

Lonneke is head of the Research department of the Eindhoven Cancer Registries, teaches Cancer Epidemiology, and is active in several (inter-)national research groups.

Selected Abstracts

Beta-blocker usage and colorectal cancer survival: a nested case-control study in the UK Clinical Practice Research Datalink cohort

Authors: B. M. Hicks, L. J. Murray, D. G. Powe, C. M. Hughes and C.R. Cardwell

Background: Epidemiological and laboratory studies suggest that beta-blockers may reduce cancer progression in various cancer sites. The aim of this study was to conduct the first epidemiological investigation of the effect of post-diagnostic beta-blocker usage on colorectal cancer-specific mortality in a large population-based colorectal cancer patient cohort.

Patients and Methods: A nested case-control analysis was conducted within a cohort of 4,794 colorectal cancer patients diagnosed between 1998 and 2007. Patients were identified from the UK Clinical Practice Research Datalink and confirmed using cancer registry data. Patients with a colorectal cancer-specific death (data from the Office of National Statistics death registration system) were matched to five controls. Conditional logistic regression was applied to calculate odds ratios (OR) and 95% confidence intervals (CI) according to beta-blocker usage (data from GP prescribing records).

Results: Post-diagnostic beta-blocker use was identified in 21.4% of 1,559 colorectal cancer- specific deaths and 23.7% of their 7,531 matched controls, with little evidence of an association (OR=0.89 95%CI 0.78, 1.02). Similar associations were found when analysing drug frequency, beta-blocker type or specific drugs such as propranolol. There was some evidence of a weak reduction in all-cause mortality in beta-blocker users (adjusted OR=0.88 95%CI 0.77; 1.00 P=0.04) which was in part due to the marked effect of atenolol on cardiovascular mortality (adjusted OR=0.62 95%CI 0.40, 0.97 P=0.04).

Conclusions: In this novel large UK population-based cohort of colorectal cancer patients, there was no evidence of an association between post-diagnostic beta-blocker use and colorectal cancer-specific mortality.

Presenter: Blanaid Hicks, Queen's University Belfast

Association between the use of statins and development of monoclonal gammopathy of un-determined significance and multiple myeloma: a case-control study within CPRD

Authors: Anderson LA*, Tapper C*, McShane CM, Landgren O, Bradley M, Hughes C, Murray LJ.

Background : Several studies have suggested statin-mediated inhibition of the mevalonate pathway is tumour-suppressive, with a pronounced effect in haematological malignancies reported. To date, there have been few investigations of the associations between statin use and monoclonal gammopathy of un-determined significance (MGUS) and/or multiple myeloma (MM). As all cases of MM arise from MGUS, preventing the development of MM provides an opportunity to combat global increases in incidence with a well tolerated class of drugs.

Methods : A retrospective case-control study using the Clinical Practice Research Datalink (CPRD) was conducted to investigate the association between prior statin use and risk of MGUS and MM among 5108 MGUS and 3801 MM patients matched to 25,333 and 18,991 controls respectively. Conditional logistic regression models, adjusted for potential confounding variables, were performed and Odds Ratios (OR) calculated excluding two years prior to MGUS or MM diagnosis.

Results: Statin users were found to have a 14% reduced risk of developing MGUS (Adjusted OR, 0.86; 95% Confidence Interval (95% CI), 0.79-0.94) and a 25% reduced risk of developing MM (OR, 0.75; 95% CI, 0.67-0.84).

Conclusions: Statin usage was associated with a reduced risk of developing both MGUS and MM in this large population-based study. The greater protective effect observed with MM, suggests statins may play a role in preventing progression of MGUS to MM or associated lymphoproliferative malignancies. Further investigation and clinical trials are however needed to confirm this.

Presented by: Charlene McShane, Queen's University Belfast

Low-dose aspirin usage after colorectal cancer diagnosis and survival: A population based cohort study

Background & Aims: A recent meta-analysis of trials of aspirin to prevent vascular events, suggest that aspirin may improve survival amongst colorectal cancer patients. We investigated post-diagnostic low-dose aspirin usage and survival in a large population-based cohort of colorectal cancer patients.

Methods: A nested case-control analysis was conducted within a cohort of 4,794 colorectal cancer patients (including 1,559 colorectal cancer-specific deaths) diagnosed between 1998 and 2007, identified in the UK Clinical Practice Research Datalink (CPRD) and confirmed by cancer registries. Colorectal cancer-specific deaths recorded by the Office of National Statistics were matched to five controls. Conditional logistic regression was applied to calculate odds ratios (OR) and 95% confidence intervals (CI) according to low-dose aspirin usage from GP prescribing records.

Results: Overall, low-dose aspirin use after colorectal cancer diagnosis was not associated with colorectal cancer-specific mortality (adjusted OR= 0.99, 95%CI 0.84-1.17; *P*=0.91) or all-cause mortality (adjusted OR= 1.01, 95%CI 0.88-1.14; *P*=0.94). A dose-response association was not apparent. For instance, low-dose aspirin use for over 1 year after diagnosis was not associated with colorectal cancer-specific mortality (adjusted OR= 0.97, 95%CI 0.79-1.20; *P*=0.80). An unplanned subgroup analysis indicated a reduction in colorectal cancer-specific mortality with low-dose aspirin use after diagnosis in stage 2 colon cancer patients (adjusted OR= 0.60, 95% CI 0.34-1.05; *P*=0.048).

Conclusions: These findings suggest that low-dose aspirin usage after diagnosis does not improve survival in all colorectal cancer patients. A possible protective effect in early stage colon cancer requires independent confirmation.

Presented by: Andrew Kunzmann, Queen's University Belfast

Poster Session Abstracts

The role of private care in the interval between diagnosis and treatment of breast cancer in Northern Ireland

Authors: Carney Patricia, Gavin Anna and O'Neill Ciaran

Objective: To examine differences in the interval between diagnosis and initiation of treatment among women with breast cancer in Northern Ireland.

Design: A cross sectional observational study.

Setting: All breast cancer care patients in the Northern Ireland Cancer Registry in 2006.

Participants: All women diagnosed and treated for breast cancer in Northern Ireland in 2006.

Main outcome measure: The number of days between diagnosis and initiation of treatment for breast cancer.

Results: The mean (median) interval between diagnosis and initiation of treatment among public patients was 18 (14) compared to 14 (11) among those whose care involved private providers. Differences between individual public providers were as marked as those between the public and private sector – the mean (median) ranging between 14 (12) and 25 (22) days. Multivariate models revealed differences were evident when a range of patient characteristics were controlled for including cancer stage.

Conclusion: A relatively small number of women received care privately in Northern Ireland but experienced shorter intervals between diagnosis and initiation of treatment than those who received care wholly in the public system. The variation among public providers was as great as that between public and private providers. The impact of such differences on survival and in light of waiting time targets introduced in Northern Ireland warrants investigation.

Aspirin use and mortality in men with localised prostate cancer: a cohort study

Authors: Evelyn M. Flahavan, Kathleen Bennett, Linda Sharp, Thomas I Barron

Background: Cyclooxygenase-2 (COX-2) expression in prostate cancer has been associated with high grade tumours and poorer prognosis. Use of aspirin, a COX-2 inhibitor, has been associated with reduced prostate cancer mortality in some studies. These studies have not, however, provided information on the dose and timing of aspirin use.

Methods: National Cancer Registry Ireland data was used to identify men with stage I-III prostate cancer (ICD10 C61) diagnosed 2001-2006. Aspirin use in the year preceding prostate cancer diagnosis was identified from linked prescription refill data (General Medical Services) and stratified by dose (low ≤75mg, high >75mg) and dosing intensity (proportion of days in that year with aspirin supply available). Cox proportional hazards models, adjusted for age, smoking status, year of incidence, comorbidity score, Gleason score, tumour size, pre-diagnostic statin use, and receipt of radiation (time-varying) were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for associations between aspirin use and all-cause and prostate cancer-specific mortality. Interactions with tumour characteristics were examined.

Results: 2,936 men with stage I-III prostate cancer were identified (aspirin users, N=1,131; 38.5%). Median patient follow-up was 5.5 years. In multivariate analyses, aspirin use was not associated with a significant reduction in prostate cancer-specific (HR 0.90, 95% CI 0.68-1.20) or all-cause mortality (HR 0.98, 95% CI 0.84-1.15). In dose response analyses, aspirin use was associated with a significantly lower risk of prostate cancer-specific mortality in men receiving >75mg of aspirin (HR 0.59, 95% CI 0.35-1.00, p=0.048) but not ≤75mg aspirin (HR 1.01, 95% CI 0.75-1.37, p=0.938). Stronger associations were also observed in men with higher aspirin dosing intensity or a Gleason score >7.

Discussion: Pre-diagnostic aspirin use, measured using objective prescription refill data, was associated with a significant reduction in prostate cancer-specific mortality in men with stage I-III prostate cancer receiving >75mg of aspirin. These results confirm previous findings, and provide important new information regarding the dose of aspirin associated with survival benefit.

Post-diagnostic Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers and risk of Breast Cancer-Specific Mortality: A Nested Case-Control Study

Authors: Úna Mc Menamin, Liam Murray, Carmel Hughes, Marie Cantwell, Chris Cardwell

Background: Preclinical studies demonstrate the anti-cancer effects of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs); however findings from epidemiological studies on cancer outcomes have been inconsistent. We aimed to further explore the relationship between ACEI and ARB use and breast cancer breast cancer-specific mortality in a population-based study.

Methods: A nested case-control study was conducted within a cohort of breast cancer patients from the National Cancer Data Repository, which was linked to Office of National Statistics death registration data and prescription records were obtained using the Clinical Practice Research Datalink. Conditional logistic regression models were used to examine the association between ACEI and ARB use and risk of breast cancer-specific mortality, adjusted for potential confounders.

Results: A total of 7,136 patients were diagnosed with breast cancer during the study period, of which 1,435 patients died due to breast cancer. During a mean follow-up of 4 years, 17% of both cases and controls received at least one ACEI prescription and 7% of both received at least one ARB prescription. Overall, no association was observed for any use of an ACEI or ARB after diagnosis (adjusted OR 1.06, 95% CI 0.89-1.26; adjusted OR 0.98, 95% CI 0.77-1.24). Results were similar by increasing number of prescriptions and cumulative defined daily doses.

Conclusions: This study, which is the largest to date and has used robust cancer registry and mortality data, showed no association between use of ACEIs/ARBs and breast cancer mortality.

Oral bisphosphonate use and subsequent risk of monoclonal gammopathy of undetermined significance and multiple myeloma: a population-based study

Authors: McShane CM, Murray LJ, Landgren O, Bradley M, Hughes C, Anderson LA

Introduction: Bisphosphonates have potent antiresorptive activity and are used as a supportive therapy for the treatment of multiple myeloma (MM). Bisphosphonates may also be prescribed to monoclonal gammopathy of undetermined significance (MGUS) patients, the premalignant precursor to MM, with osteoporosis. Emerging *in vitro* and clinical evidence suggests bisphosphonates may have antimyeloma properties.

Methods: Using the UK Clinical Practice Research Datalink (CPRD), a nested case-control study was undertaken to investigate the association between antecedent oral bisphosphonate use and risk of MGUS/MM. Conditional logistic regression models were used to estimate odds ratios (OR) and associated 95% Confidence Intervals (CI) excluding 2 years prior to MGUS/MM diagnosis. Findings were adjusted for a number of potential confounders including age at diagnosis, comorbidities including rheumatological diseases, prior cancer, number of GP consultations and lifestyle variables.

Results: In total, 5,108 MGUS and 3,801 MM patients matched to 25,333 and 18,991 controls respectively were identified. In adjusted analyses, individuals prescribed bisphosphonates were significantly more likely than their matched controls to develop MGUS (adjusted OR, 1.28, 95% CI 1.13-1.47) while a nonsignificant increased risk was observed for MM (OR 1.13, 95% CI 0.93-1.37).

Conclusion: In this large population-based study investigating bisphosphonate use and risk of MGUS/MM, an increased risk of MGUS was observed. As MGUS is typically incidentally diagnosed this finding is most likely attributable to detection bias. It has been speculated that early use of bisphosphonates may delay progression of MGUS to MM. Further investigation looking at the role of bisphosphonates and MGUS progression is underway.

Non-steroidal anti-inflammatory drug use and cervical cancer risk: a case-control study nested in the Clinical Practice Research Datalink

Authors: Wilson JC§, O'Rorke MA§, Glover JA, Murray LJ, Hughes CH, Gormley, GJ, Anderson, LA.

§ Joint first authors

Purpose: Non-steroidal anti-inflammatory drugs (NSAIDs) have many anti-carcinogenic properties via the inhibition of cyclooxygenase 2 (COX-2). Only one study, a cohort study examining risk of all cancers, investigated their role in cervical cancer with inconsistent findings between non-aspirin NSAIDs and aspirin. The aim of this study was to further investigate NSAID/aspirin use and cervical cancer risk.

Methods: Using the United Kingdom Clinical Practice Research Datalink, 724 women diagnosed with cervical cancer between 1st January 1995 and December 2010 were compared to 3,479 women (without cervical cancer) matched on year of birth and general practice. Conditional logistic regression analysis adjusted for smoking, sexually transmitted infections, HRT and contraceptive use, was used to calculate odds ratios (OR) and 95% confidence intervals (CI) for cervical cancer risk among users of any oral NSAIDs, non-aspirin NSAIDs and aspirin, as assessed from primary care prescribing data.

Results: Excluding the year prior to diagnosis, there was no association in adjusted analyses between ever vs. never use of an NSAID (OR 0.92, 95% CI 0.77-1.09), non-aspirin NSAID (OR 0.95, 95% CI 0.80-1.13) or low-dose aspirin (OR 1.07, 0.80-1.44) and cervical cancer risk. In analysis of daily defined doses, there was no association with cervical cancer risk comparing the highest users to non-users of NSAIDs (OR 0.98, 95% CI 0.69-1.39) or non-aspirin NSAIDs (OR 1.00, 95% CI 0.70-1.43) or low-dose aspirin (OR 1.04, 95% CI 0.59-1.81).

Conclusion: This large historical cohort study found no evidence of an association between non-aspirin NSAID or aspirin use and cervical cancer risk.

Beta adrenergic receptor expression and beta-blocker use: association with breast cancer survival and prognosis (protocol)

Authors: O'Rorke M*, Cardwell C, Hughes C, Cantwell M, Powe D, Salto-Tellez M, Murray L.

Background: Breast cancer is the most commonly diagnosed cancer, and second most common cause of cancer death amongst UK women; highlighting the importance of identifying treatments that may impact upon survival. Epidemiological evidence suggests beta-blockers (β-blockers) might favourably affect cancer survival and recurrence. However, studies that have examined this association to date have been largely small in size, reporting inconsistent findings with respect to the selectivity of β-blockers.

Aim: To investigate the prognostic significance of tumour beta-adrenergic receptor (β-AR) expression and post-diagnostic β-blocker use with breast cancer specific survival.

Methods: Using a nested case-control study design, patients who have died from breast cancer (cases) between 1st January 2009 and the 31st December 2015 in Northern Ireland will be matched on age, tumour stage and year of diagnosis to breast cancer patients who are alive at the cases' point of death (controls). Tumour blocks will be retrieved and used to construct tissue microarrays for characterisation of β-AR expression via immunohistochemistry. Conditional logistic regression analyses will be used to compare the risk of cancer-specific death by 1) β-AR expression and 2) β-blocker use generating odds ratios (OR) and 95% confidence intervals (CI) adjusting for various potential confounders.

Impact: By being the first study to examine the interaction between β-AR expression and β-blocker use, this study may lead to a better indication of breast cancer patients at risk of cancer progression and will provide robust information on the potential for therapy with β-blockers in such patients.

Funding: *CRUK Population Research Postdoctoral Fellowship

Effects of metformin and sulfonylureas on overall and colorectal cancer-specific mortality

Authors: Spillane SC, Bennett K, Sharp L, Barron TI.

Background: Preclinical studies suggest a role for metformin in colorectal cancer (CRC) treatment. Associations between metformin exposure and mortality are assessed in this population-based study.

Methods: National Cancer Registry Ireland records linked to prescription claims data were used to identify stage I-IV CRC patients diagnosed 2001-2006. Exposure was classified by receipt of a prescription for metformin +/- a sulfonylurea (MET) or a sulfonylurea alone (SUL) in the 90 days pre-diagnosis. Cox proportional hazards models were used to estimate hazard ratios for mortality in MET vs SUL groups, adjusted for age, sex, stage, grade, site, comorbidities, diagnosis year, and insulin/aspirin/statin exposure.

Results: 5,617 stage I-IV CRC patients were identified; 369 received metformin and/or sulfonylureas (MET: n=257; SUL: n=112). Metformin was associated with 28% lower all-cause mortality (HR 0.72, 95%CI 0.53-0.98) and a non-significant 24% reduction in CRC-specific mortality (HR 0.76, 95%CI 0.52-1.13). In analyses stratified by tumour site, metformin was associated with 34% lower all-cause mortality for colon cancer (HR 0.66, 95%CI 0.46-0.95). No association was observed for rectal cancer. Associations between metformin and reduced mortality were stronger for early stage (I/II) disease.

Conclusions: Metformin exposure was associated with significantly reduced mortality in diabetic patients, particularly in colon tumours or early stage cancer.

Notes