SYSTEMATIC REVIEW OF EFICACY OUTCOMES REPORTED IN RANDOMISED CONTROLLED TRIALS OF FIRST-LINE (1L) THERAPIEYS FOR METASTATIC BREAST CANCER (mBC)

Harms C1, McGregor IA2, Salani E1
1Complete Medical Group, Glasgow, UK, 2Complete Medical Group, Placelstef, UK, T. Hoffmann—La Roche Ltd, Basel, Switzerland

OBJECTIVES: There is currently some debate around the optimal role of overall survival (OS) as a gold standard in assessing the benefits of oncology products. The objective of this analysis was to provide evidence to inform this discussion from a review of the clinical outcomes in 1L mBC trials reported over the last 10 years.

METHODS: MEDLINE and Cochrane databases were searched to identify randomised controlled trials of 1L mBC published between January 1998 and February 2009. Studies in exclusively human epidermal growth factor receptor 2-positive populations were excluded. RESULTS: Clinical efficacy data were extracted from 36 trials. All 36 trials reported response rate (RR), 34 reported a progression-free end point and 33 reported OS. The most commonly stated primary efficacy end points were progression-based; only 6 trials stated OS as the primary end point. Improvement in median OS ranged from 0.1 to 7.8 months, improvement in median progression-free survival (PFS) ranged from 0.1 to 6.4 months and improvement in RR ranged from 0.3 to 2.8. Fourteen trials (39%) reported a significant progression-based benefit, 4 of which (36%) reported significant median OS. Each of these 4 trials also reported a significant benefit in RR and median PFS. CONCLUSIONS: Overall, very few 1L mBC trials have reported a significant median OS benefit. Where a significant OS benefit was reported, a significant overall RR and PFS benefit was also reported. These findings are an important light of the ongoing debate on the relevance of currently used clinical end points in mBC trials.

STANIN USE AND THE RISK OF COLORECTAL CANCER: A POPULATION-BASED COHORT STUDY

Ceccarelli M1, Maio V2, Sabaggh S2, Rabonwitz C2, Diamond J2
1Università degli Studi di Firenze, Firenze, Italy, 2Thomas Jefferson University, Philadelphia, PA, USA

OBJECTIVES: Basic scientific evidence suggests that statins inhibit the growth of colon-cancer cell lines, and secondary analyses of some randomized clinical trials suggest that they reduce the risk of colorectal cancer. However, evidence from observational studies has been conflicting on whether the risk of colorectal cancer is reduced in statin users. We sought to assess the association between statin use and the rate of colorectal cancer in a large cohort of residents in Emilia-Romagna, Italy.

METHODS: We conducted a population-based cohort study using the longitudinal health care database of Emilia-Romagna, Italy, a region with approximately 4.2 million inhabitants. This comprehensive database contains information on all health care services rendered to the population, including hospital, outpatient pharmacy and specialty data. We identified all initiators of statins; initiators of glaucoma medications served as a comparison group. Colorectal cancer cases were identified by hospital discharge data. Multivariable logistic regression analyses were used to adjust for confounding. RESULTS: Patient characteristics were similar in both groups, but statin initiators (30,534) were prevalently male, were slightly younger, and used hospital services more frequently than glaucoma medication initiators (78,361). During a maximum of 3 years of follow-up, the incidence rate of colorectal cancer was lower in the statin users than in the glaucoma medication users (0.49% vs. 0.79%; Relative Risk, 0.69, 95% CI, 0.52 to 0.92). The adjusted odds ratio for statin use compared with nonuse was 0.67 (95% CI, 0.57 to 0.79). During the maximum of 3 years of follow-up, the incidence rate of colorectal cancer was lower in the statin users than in the glaucoma medication users (0.49% vs. 0.79%; Relative Risk, 0.69, 95% CI, 0.52 to 0.92). The adjusted odds ratio for statin use compared with nonuse was 0.67 (95% CI, 0.57 to 0.79). During the maximum of 3 years of follow-up, the incidence rate of colorectal cancer was lower in the statin users than in the glaucoma medication users (0.49% vs. 0.79%; Relative Risk, 0.69, 95% CI, 0.52 to 0.92). The adjusted odds ratio for statin use compared with nonuse was 0.67 (95% CI, 0.57 to 0.79). During the maximum of 3 years of follow-up, the incidence rate of colorectal cancer was lower in the statin users than in the glaucoma medication users (0.49% vs. 0.79%; Relative Risk, 0.69, 95% CI, 0.52 to 0.92). The adjusted odds ratio for statin use compared with nonuse was 0.67 (95% CI, 0.57 to 0.79).

Castration-resistant prostate cancer (CRPC): A UK population study

Morgan C1, McInroy P2, Chamberlin G2, Cabrera C2, Parry D2
1Cardiff Research Consortium, Cardiff, UK, 2AstraZeneca, Malmö, Sweden, AstraZeneca, Placelstef, UK

OBJECTIVES: To determine the epidemiology of castration-resistant prostate cancer (CRPC). METHODS: Primary care data for males aged ≥40 years with a diagnosis of prostate cancer (PC) based on the Read classification were selected from The Health Improvement Network (THIN) between 1998 and 2008. Patients with CRPC were defined by a Read code indicative of medical/surgical castration and evidence of increasing levels of prostate specific antigen (PSA) following hormone/androgen therapy. Incidence and mortality rates were based on person years at risk. Survival was estimated using Cox regression analyses. To compare survival between CRPC and non-CRPC, non-CRPC controls were matched by age, year of diagnosis and baseline survival. RESULTS: Between 2003/2007, 8,678 patients with PC were identified. Incidence was 22.4 per 10,000 patient years and prevalence was 153.0 per 10,000 patients. 969 patients (11.2%) progressed to CRPC. Amongst patients with PC the prevalence was 1,530 per 10,000 cases. Rate of first recorded metastases was 34.9 per 1,000 patient years for CRPC; compared with 24.8 for non-CRPC. Following CRPC onset, the mortality rate was 201.2 per 1,000 patient years compared with 86.7 per 1,000 for non-CRPC. Based on matched data, the hazard ratio for CRPC relative to non-CRPC was 2.61 (p < 0.001). Extrapolated to the UK the data from this study would predict approximately 220 CRPC and 2,600 PC with metastatic metastatic spread. Similarly the annual incidence would predict approximately 37,000 PC, 8,400 CRPC and 820 CRPC with recorded metastatic spread. CONCLUSIONS: The extrapolated prevalence and incidence estimates of PC are comparable to other studies in the UK. CRPC status was associated with a significantly greater rate of metastases and mortality. Due to the reliance on PCA readings in defining CRPC status it is acknowledged that we may underestimate the incidence of CRPC.

BREAST CANCER PATIENTS ARE TWICE AS LIKE TO DEVELOP ARTERIAL THROMBOEMBOLIC EVENTS AFTER DIAGNOSIS COMPARED TO CANCER-FREE WOMEN

Shantakumar S1, van Hark-Sukal MPP2, Nelison J2, Kamphuisen PW3, Abrahamson PE4
1Glucomitekline, Research Triangle Park, NC, USA, 2PHARMO Institute for Drug Outcomes Research, Utrecht, The Netherlands, 3Academic Medical Center, Amsterdam, The Netherlands, 4Salmon Bay Epidemiology, Seattle, WA, USA

OBJECTIVES: To study occurrence of arterial thromboembolic events before and after breast cancer (BC) diagnosis compared to cancer-free controls as this information is lacking in phantom literature. METHODS: Women who had a first hospitalization for BC between 2002 and 2007 were selected from the PHARMO Record Linkage System, which includes drug use and hospitalization data of approximately 3 million residents in the Netherlands. BC patients were matched 1:10 by age with cancer-free controls, with a maximum of 5 years of follow-up. BC patients were defined by a Read code indicative of medical/surgical castration and evidence of metastases. CONCLUSIONS: BC patients were twice as likely to develop ATEE compared to cancer-free controls (Hazard Ratio = 1.7 [95% CI:1.3–2.1]). This risk was attenuated but remained statistically significant after adjusting for prior cardiovascular or TEE hospitalization and prior antithrombotic or cardiovascular drug use (Hazard Ratio = 1.3 [95% CI:1.0–1.7]). Independent risk factors for developing ATEE included age (HR 1.04 per year, p = 0.001), prior use of antihypertensives or antiplatelet drugs (HR 1.36 per prior use, p = 0.001), and prior use of antithrombotic or cardiovascular drug use (HR 1.27 per prior use, p = 0.001).