BS34 ANTIPLATELETS AND RISK OF CANCER: A NATIONAL PROPENSITY-SCORE WEIGHTED COHORT ANALYSIS

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Introduction Common cardiovascular therapies have been suggested to have a protective effect against cancer. Aspirin, an antiplatelet, has been shown to reduce the incidence of some cancers, possibly because platelets are needed for tumour cells within a solid cancer to survive. The effect on cancer incidence of newer antiplatelets, such as thienopyridine inhibitors like Prasugrel and P2Y12 inhibitors like Ticagrelor is unclear.

Methods The Virtual Cardio-Oncology Research Initiative (VICORI) data resource of linked English national cancer and cardiovascular disease audits was used to assess the risk of total cancers as well as breast, colorectal, lung, and prostate cancer for myocardial infarction patients who had received thienopyridine inhibitors or ticagrelor during admission between 2000–2018. Time-varying Cox proportional hazards regression models estimated the risk of the outcomes for individuals who received the medications compared to those who did not. Propensity score weights were used to adjust for differences between individuals who did and did not receive the relevant medication.

Results Among 228,495 cardiac patients, those discharged on thienopyridine inhibitors were at lower risk of cancer than those who did not, HR=0.90 (0.84–0.96). Cancer risk for individuals discharged on thienopyridine inhibitors was lowest in the first year after discharge. There were no differences in risk of breast, colorectal, prostate or lung cancer by thienopyridine inhibitors. Ticagrelor was not associated with risk of cancer, HR=0.96 (0.89–1.04) and the risk of cancer over time for individuals discharged on ticagrelor did not vary over time. Ticagrelor was associated with a lower risk of breast cancer, HR=0.60 (0.40–0.92), but not colorectal, prostate or lung cancer.

Conclusions Cardiac patients who received thienopyridine inhibitors were at lower risk of cancer, and those who received ticagrelor were at lower risk of breast cancer, specifically. These findings should be further validated in large-scale cohort studies and prospective clinical trials.

BS35 THE ROLE OF THE LNCRNA EINCR1 AND MAPK SIGNALLING IN THE HEART

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The mitogen-activated protein kinase pathway (MAPK) transduces signals to affect a variety of biological processes, including proliferation, differentiation, and cellular survival. It is known to be key during cardiovascular development and during physiological cardiovascular function, indicated by the congenital heart defects that are typical of Noonan syndrome and other diseases that affect MAPK signalling. A previous group have shown that a long non-coding RNA, the EGF-inducible non-coding RNA 1 (EINCR1) regulates the MEK/ERK branch of the MAPK pathway, which usually responds to growth factors and other mitogenic signals. However, the exact mechanism is unknown. Due to the importance of the MEK/ERK pathway in various cardiovascular physiological and pathologi- cal processes, and because EINCR1 expression is highest in the heart, we wanted to investigate how EINCR1 regulates the MEK/ERK kinase cascade. Current pharmacological inhibitors of the MEK/ERK pathway have significant side effects, and the identification of alternative regulatory mechanisms could prove to be beneficial for patients with a variety of diseases. In the first phase of this study, we had three main aims. First, to confirm that EINCR1 expression is induced by MAPK activation via EGF treatment and transfection with a constitutively active MEK. Second, to characterise the EINCR1 locus using Nanopore long-read sequencing because previous studies have suggested that the current gene annotation is not complete. Finally, we aimed to identify any enhancers in the locus that could be contributing to its regulatory effects, and once identified, to use CRISPRi to downregulate the activity of these enhancers and use RT-qPCR to identify the genes affected. First, we confirmed that EINCR1 expression is induced following EGF treatment. Nanopore sequencing then revealed that the transcripts that arise from the EINCR1 locus are not well defined, with no consistent spliced structure, like other lncRNAs, such as MALAT1. The enhancer assays indicated that two regions near the EINCR1 locus have potential enhancer ability when compared to a random region of DNA that was used as a control. Our initial findings indicate that MAPK signalling activates enhancers near and within the EINCR1 gene body. Nanopore sequencing revealed that the EINCR1 transcript lacks a consistent splicing pattern in a bladder cancer cell line. However, future studies are aimed at assessing the structure of the EINCR1 transcript in the heart, as there is some evidence that suggests it may be consistently spliced in the cardiomyocytes. A consistent structure in the heart is important to verify that the transcript is functional in addition to the enhancers. Analysis of our CRISPRi work is ongoing, and we hope to identify genes that are regulated by this locus soon. Understanding the entire MAPK signalling pathway, including its regulatory mechanisms, could be key in the prevention of disease and for the development of novel treatments of cardiovascular diseases.

BS36 ACUTE ARTERIAL HAEMODYNAMICS ACTIVATION OF ENDOTHELIAL TO MESENCHYMAL TRANSITION IN LONG SAPHENOUS VEINS. IMPACT ON VEIN GRAFT DISEASE

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Introduction The long saphenous vein (LSV) is frequently used in cardiac surgery; however, its use is complicated by late stenosis or occlusion due to the development of intimal hyperplasia (IH). TGF-β has been implicated in the process of IH