Title: Antithrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease

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Introduction:

The co-occurrence of coronary artery disease (CAD) and atrial fibrillation (AF) is common. While guidelines and supporting data exist on optimal anti-platelet/anti-coagulant strategies for ≤12 months (acute) after intervention (PCI or CABG), evidence regarding long-term(stable) therapy is limited.

Design and Methods:

The study was a multi-centre (Japanese), open-label trial. Patients with AF who had under gone PCI/CABG ≥12 months ago or angiographically-confirmed CAD (stenosis ≥50%) were randomized to rivaroxaban with/without an anti-platelet. The primary efficacy end point was a composite (stroke, systemic embolism, myocardial infarction, unstable angina requiring revascularization, or death from any cause) (analysed for non-inferiority). The primary safety endpoint was major bleeding (analysed for superiority).

Results:

The study was halted early given increased mortality in the combination group. Rivaroxaban monotherapy was non-inferior for the primary efficacy endpoint (HR 0.72; 95% CI 0.55-0.95; P<0.001) and was found superior (P=0.02). Rivaroxaban monotherapy was superior for the primary safety endpoint (HR 0.59, CI 0.39-0.89; P=0.001).

Conclusions:

For those with stable CAD and AF, monotherapy with rivaroxaban is non-inferior to combination with anti-platelets and leads to less major bleeds.

Discussion Strengths and Limitations:

The study explores a relevant clinical question encountered day-to-day, albeit in only one direct oral anti-coagulant (DOAC). The strengths were the design (randomised control trial (RCT)), good randomisation, sufficient enrolment and funding. The weaknesses acknowledged were the open-label nature, relatively high rates of withdrawal/loss of patients, early termination (perhaps leading to over-estimation of efficacy), doctor choice for anti-platelets and the single-country setting with an unusual local dose (although likely similar active dose). Personally, anon-stated significant limitation was, given pharmaceutical funding from Bayer, it only used rivaroxaban limiting its applicability.

Reflections and Future Directions:

The study is relevant to medical trainees given the common co-occurrence of CAD and AF and increasing use of DOACs. Teams often choose to hold anti-platelets based on European Society of Cardiology

guidance, although this guidance was based on observational data. RCT evidence should further alert, especially in older patients with pill-burdens and in those with higher bleeding risks.

RCTs are required in multiple settings and of other DOACs to cement this as a class I recommendation (in Ireland, especially apixaban as it is the MMP DOAC of choice and most used). Furthermore, it will be interesting to see if superiority is replicated for similar efficacy end points because it is somewhat counter-intuitive that less anti-thrombotic therapy leads to fewer cardiovascular events/deaths.