Title: Anti-thrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease (AFIRE Study) Journal article review

Study:

This open-labelled, randomised, parallel-group study [CITATION Yas19 \l 6153], undertaken in 294 Japanese centres with 2200 patients, was precipitated by guidelines with insubstantial data on the practice of anti-thrombotic therapy on patients with atrial fibrillation (AF) and stable coronary artery disease (CAD). The study compared rivaroxaban monotherapy vs rivaroxaban and single anti-platelet therapy with the above cohort.

The primary efficacy end-point, cardiovascular events and deaths from any cause, showed monotherapy (event rates of 4.14% per patient-year) was non-inferior (P<0.001) to combined therapy (5.75%), using modified intention-to-treat approach with a non-inferiority margin of 1.46, (hazard ratio, 0.72; 95% confidence interval [CI], 0.55 to 0.95). Monotherapy (1.62%) was superior (P=0.01) to combination therapy (2.76%) for the primary safety end point of major bleeding (hazard ratio, 0.59; 95% CI, 0.39 to 0.89).

Patient selection:

Any gender ≥20 years old with non-valvular AF and stable CAD with CHADS2 ≥1, with 1 of the following:

1. PCI or

2. CABG ≥1 year ago or

3. Coronary stenosis ≥50% not requiring PCI.

Conclusion:

Rivaroxaban monotherapy was non-inferior to combination therapy for efficacy and superior for safety in this patient population.

Interpretation:

The study was based on the concept that the two conditions could be treated less intensively. The study has a gender and ethnicity bias as the patients are pre-dominantly male (79%) and Japanese. The genetic difference in Asians and non-Asians is known in regards to bleeding and stroke [CITATION Tze16 \l 6153], while the minority percentage of females in CVD studies is well documented [CITATION Ham11 \l 6153].

The open label allows to introduce bias as does the anti-platelet choice being decided by individual physicians. The anti-platelet choice leaves this study open to scrutiny. With the modest sample group and early termination of the study, the efficacy data may be overestimated. Pairing that with the

unpredicted reduction in ischaemic events and death from monotherapy emphasises the query of the play of chance in this study.

Reflection:

Although, the study is confined to the participant's ethnicity and male gender majority, I believe our practice in Ireland will be influenced by this study's result. Certain physicians will believe extrapolating the conclusions of this study to an Irish population may be detrimental. Supporting this concern, we have access to the analysed data from PIONEER AFPCI [CITATION Gib16 \l 6153], RE-DUAL PCI [CITATION Can17 \l 6153], and AUGUSTUS [CITATION Lop19 \l6153] trials, which established the safety of dual therapy in stable CAD patients with AF and certain physicians will want to see established non-inferiority data in Caucasians before following the guidelines.

The AQUATICA trial, in France, will help to resolve the problem of antithrombotic therapy in European patients with stable CAD and AF. The overall effect of this trial in terms of the HSE is that it would hopefully decrease the burden of iatrogenic major bleeding, decrease polypharmacy, decrease overall cost to the patient and HSE while ensuring the decrease of DALYs for patients.

References:

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