Dr Edmund Lee
MBBS (WA) FRACP FCSANZ
CARDIOLOGIST
Provider # 504628LK

Tel 6169 2060
elreception@wacardiology.com.au

Dear Colleague,

I trust this summary of the most recent cardiology trials will be of interest to you in your practise.

TOP 10 TRIALS OF 2023

1) SELECT TRIAL

Semaglutide 2.4mg in a large 17,604 RCT with established CAD, without diabetes and a BMI greater than 27 showed a 20% reduction in CV death, nonfatal MI or nonfatal stroke at a mean follow-up of 40 months. Oral semaglutide is now available in other countries with similar HbA1c reductions compared to liraglutide with greater reductions in HbA1c compared to SGLT2 antagonists. Greater weight loss was achieved with semaglutide compared to liraglutide. Downsides include GI intolerance and costs. The recently published results of the SURMONT-4 withdrawal trial underscores the challenge of weight regain when the drug is stopped.

Two meta-analyses have shown that Tirzepatide (dual GLP-1 and GIP receptor agonist) to be more effective in weight loss. We eagerly await trials demonstrating CV protection.

2) NOAF-AFNET 6 and ARTESIA

These 2 trials have challenged the idea of anticoagulation in patients with subclinical AF detected on implantable cardiac devices. NOAF-AFNET randomly assigned 2500 patients over the age of 65 lasting for at least 6 minutes detected by cardiac implanted devices who had at least one additional risk factor for stroke. The mean duration of AF was 2.8 hours. The trial was stopped early at 21 months because of perceived excess bleeding in the edoxaban arm (31% increased risk, or 5.9% per patient-year vs 4.5% per patient-year). There was a small 19% reduction (4% vs 3.2% per patient-year) in the primary endpoint of stroke, systemic embolism and CV death.

ARTESIA randomly assigned 4000 older patients with short lived device detected AF to apixaban vs aspirin (median duration, 1.5hours). After 3.5 years, Apixaban reduced the primary endpoint of stroke and systemic embolism by 37% (0.78% per patient-year vs 1.24% per patient-year) but increased major bleeding by 80% (1.71% per patient-year vs 0.94% per patient-year).

Both trials demonstrated a reduction in thrombotic events but an increase in bleeding rates. The biggest discovery was the low stroke rates in both trials. What we need now is an analysis correlating duration of AF and net clinical benefit. Some experts have suggested using 24 hours as a cut-off.

3) ORBITA-2

This trial randomised 300 patients with stable coronary artery disease without anti-anginal therapy to PCI or placebo-PCI (sham control arm). Not surprisingly, the mean anginal symptom score was significantly lower in the PCI group.

4) PARTNER 3 – 5 YEAR FOLLOW-UP AND EVOLUT 4 YEAR RESULT

Longer term data on TAVR (Transcatheter aortic valve replacement) in low-risk surgical patients were published. In the PARTNER 3 trial of balloon expandable TAVR, the short-term benefit of TAVR neutralised over time. Death, stroke and rehospitalisation were all similar and valve haemodynamics matched those of surgical implanted valves. There was more aortic regurgitation in the TAVR arm.

The Evolut low risk 4-year results for self-expandable TAVR still demonstrated a benefit for death and stroke compared to SAVR (Surgical aortic valve replacement). Valve haemodynamics were also better in the TAVR arm. New permanent pacemaker rates remained higher in the TAVR arm.

Both trials will continue to follow patients.

5) CLEAR-OUTCOMES TRIAL

This trial randomised 14000 patients at increased CV risk, who are intolerant or unwilling to take statins to bempedoic acid vs placebo. At a median duration of 40.6 months, there was a 0.75mmol/L reduction in LDL. There was a 13% relative reduction in death, MI stroke and revascularisation – 1.6% absolute risk reduction. This gives us another alternative to those who are unable to take statins. Other options now include Inclisiran (awaiting large ORION -4 trial) and oral PCSK9 inhibitors (showed good reductions in LDL in phase 2 trial).

6) ATTRibute CM STUDY

Transthyretin amyloid cardiomyopathy is now getting diagnosed more frequently. It is a rare progressive fatal disease caused by the accumulation of misfolded transthyretin protein in the heart. Previously, the ATTR-ACT trial of tafamidis demonstrated a reduction in all cause mortality, CV hospitalisation and decline in functional capacity by 6-minute walk distance and QOL assessed by Kansas City Questionnaire. Acromadis is a superior stabiliser compared to tafamidis in vitro.

This trial randomised 632 patients in a 2:1 ratio to acromadis to placebo. At the end of 30 months, there was a significant reduction in all-cause mortality by 25% and 50% reduction in CV hospitalisation. There was also a significant reduction in BNP, 6-minute walk and quality of life.

7) STEP-HFpEF

The placebo-controlled trial of semaglutide in obese patients with HFpEF was unblinded and too small to conclude much about the outcomes but at least hinted at the safety in HFpEF. Not surprisingly, obese patients with HFpEF felt better if they lost weight.

8) ILUMIEN IV, OCTOBER, RENOVATE-COMPLEX PCI, OCTIVUS TRIAL

These trials highlight advances in intracoronary imaging to guide stent placement in more complex coronary lesions.

9) ELAN STUDY

This study showed that starting DOAC treatment sooner (within 48 hours of a minor or moderate stroke and on days 6-7 following a major stroke) was not associated with an increased risk of intracranial haemorrhage with a lower incidence of reducing further ischaemic events.

10) TRILUMINATE

Finally, a trial on tricuspid clip in patients with symptomatic severe TR was positive on quality-of-life improvement. Death was not reduced or even hospitalisation for heart failure. It was also not a sham-control study.