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Questions & Answers with Dr. David Fitchett

The changing landscape of secondary prevention

1. *and 7. Why can't PCSK9i be started without ezetimibe. My understanding is that the actual (not surrogate) endpoint improvements with ezetimibe are not as great as the pharma would have us believe?*

   Answer: I agree that it makes little sense to require ezetimibe treatment before considering a PCSK9 inhibitor especially when the LDL level is far from target or the treatment is for very high CV risk reduction. Ezetimibe reduces LDL by 15% whereas PCSK9i by at least 50% on top of the effect of maximal statin therapy. You are correct that the CV benefit of adding ezetimibe to a statin was modest in the Improve It trial: and it took 7 years to show benefit

   The main reason for adding ezetimibe in high risk patients or those who fail to achieve targets is to satisfy insurers and ODP for reimbursement. I agree in most cases it makes no sense, and would not be a requirement if the cost of a PCSK9i was the same as ezetimibe

2. *also, the fact that using Icosapentyl ethyl is so beneficial begs the question shouldn't we be addressing contributors to TGs such as carbs and EtOH, not just lipids? dietary i mean. It seems that cardiology still isn't addressing the CHO role in diet*

   Answer: Yes we should address causes of an elevated TG such as diabetes / metabolic syndrome, obesity, and alcoholism. Weight loss and alcohol abstinence remain very important. However, many people with an elevated TG have no clear cause. Icosapent ethyl is beneficial in patients with elevated TG BUT the benefit does not relate to the amount TG is reduced. It is possible the benefit of Icosapent ethyl is not through TG reduction.

3. *ticagrelor 60mg is not covered by ODB,*
4. *Ticagrelor 60mg is not covered by ODB-any suggestions*

   Answer: Unfortunately, we shall have to wait until ODB approval is forthcoming. I am sure their reluctance is a budgetary issue.

5. class action suit against rivaroxaban in US decreases patient acceptance. Comments?

   Answer: The class action suit relates to the drug causing bleeding in the absence of an antidote. Even in the absence of an antidote rivaroxaban is safer than warfarin. The most feared complication of anticoagulation is an intra cerebral bleed (ICB). In the ROCKET trial the rate of ICB in patients taking rivaroxaban was 50% that of the patients on Warfarin. Although vitamin K and coagulation factor concentrates reverse anticoagulation with warfarin, they take time to administer and by the time the agents have had an effect, it I often too late to save life or brain.
   I reassure patients that life threatening bleeding is much less with rivaroxaban, and if you have a serious bleed with warfarin antidote may not be effective fast enough to save you. I would rather prevent bleeding with a NOAC than use as unreliable agent such as warfarin.

6. and *8 Why is nobody talking about TACT trial, (chelation therapy) in DM patients with MI which showed RRR of 50% (with Max vitamins) and NNT of 6 to prevent MACE, TACT2 is in process but we should prepare to offer chelation in future (PI Dr. G. Lamas)*

Answer: There is one large clinical trial TACT that showed a modest benefit of chelation therapy in patients with heart disease. The benefit was largely due to a reduction of coronary revascularisation. The primary endpoint was marginally statistically significant, there were high drop-out rates, and concerns about potential unblinding. Equal numbers discontinued treatment because of adverse effects in the treatment and placebo arms and there were no significant differences in serious adverse effects.
Because of concerns about the conduct of the trial, and the marginal benefit, the FDA have not given approval for chelation therapy for CV benefit. The TACT 2 trial is underway in patients with diabetes and CVD. Until that reports it is premature to offer chelation therapy to patients with heart disease.

7. *so why is that, that we have to use Ezitimibe? seems there should be a lobby eliminating this step!*
   See above **– RESPONSE UNDER QUESTION 1**

8. *conclusion on chelation and toxicity not true. There were more serious adverse events in the placebo group than in the chelation group. Very safe.*

   See above

9. *Is the decrease in CV events by SGLP2i is confined to Empagliflozin only or it is class effect and if so is it only for 2ry prevention or for primary prevention.*

   Answer: The results of the EMPA REG Outcome, Declare, Canvas and Credence trials all show CV benefit with significant reductions of the primary (or co-primary endpoint). All showed reduction of heart failure hospitalisation. In the studies with the highest risk populations (EMPA REG Outcome and CREDENCE) CV mortality was reduced. So it is very likely that the CV benefit of SGLT2 inhibitors is a class effect and most of the differences observed in the four trials are due to differences in the treatment populations. However, differences between the three agents tested cannot be excluded without a head to head trial that is unlikely to occur.
   Both Canvas and Declare had patients with and without cardiovascular disease. In the patients with only risk factors (ie Primary Prevention group) CV events were unchanged, yet heart failure hospitalisation was reduced. The CV benefit appears to be greatest in patients with established CV disease.