ST. MICHAEL'S
UNITY HEALTH TORONTO

Questions & Answers with Dr. Kim Connelly

Diabetes management: focusing on CV outcomes

1. Where is metformin on the table?

Answer: Metformin has no current trials to assess its role for CV safety – all current trials were performed ON TOP of Metformin. Hence it does not appear on the table.

At present, apart from EASD/ESC document, all other groups recommend metformin and diet/lifestyle as first line, then SGLT2i /GLP1RA as appropriate.

2. Do we need to take the risk of ampuation from SGLT-2 inhibitors into account when prescribing for a patient with PAD?

Answer: The risk of amputation was only seen in high risk persons (i.e. prior amputation), in the CANVAS trial with canagliflozin. It has not been seen with other SGLT2i. I would avoid using these agents in persons with critical limb ischemia i.e pre amputation, but otherwise no concern with PAD.

3. In what cases would we prescribe a GLP-1 over an SGLT-2?

Answer: In those with heart failure or renal dysfunction – SFGLT2i are preferred. In those where weight loss and anti atherosclerotic effects are preferred, a GLP1RA is preferred. SGLT2i also have bigger reduction in BP i.e. 5-6mmHg reduction.

Finally, cost and injection are other features which may influence choice.

4. if a patient has diabetic retinopathy, would you use Ozempic

Answer: YES, overall safety clearly established, and benefits far outweigh extremely small visual risk.

5. What is the evidence for dose of SGLt2 in DM1 by "Endocrnologists"? Thx

Answer: A number of trials have been done with dapagliflozin and sotiglaflozin. However, the risks of diabetic ketoacidosis remain much higher, hence only highly selected persons, with close follow up should be considered for this. It is important to note the FDA has NOT approvied SGLT2i for persons wioth type 1 DM, but the EMA has approved these agents for Type 1 DM.

6. Why don't we have any RCT comparing SGLT-2i with GLP-1 agonists or members of one class against each other, or a strategy using some of the new drugs AGAINST an insulin strategy? In Covid-19, WHO and others have rapidly organized publicly-financed studies to answer such important questions. Why are we denied such studies in diabetes, which is a much more common problem, just because it would not be in the interests of manufacturers ... could CCS and CDA possibly put aside commercial interests and advocate for real world practical trials that might show us the best way to treat DM2 ???

Answer: Tough – it comes to $$. These trials are extremely expensive. Most of the ongoing GLP1RA trials will have a high percentage of people on a SGLT2i, so that may help address this question.

7. Risk of aggravating claudication in SGLT-2 inhibitor introduction in T2DM

Answer: The risk of amputation was only seen in high risk persons (i.e. prior amputation), in the CANVAS trial with canagliflozin. It has not been seen with other SGLT2i. I would avoid using these agents in persons with critical limb ischemia i.e pre amputation, but otherwise no concern with PAD.

8. IF SOMEONE HAS SUFFERED from ketoacidosis from sglt2 inhibitors can they be restarted at a later date?

Answer: Yes, however it must be individualised – if there is a clear precipitant then it may be safer to reintroduce, but if there is no obvious precipitant or if issues with communication etc then it may be safer to avoid. Overall very uncommon.

9. Has the FDA approved use of SGLt2 in Type 1 DM?

Answer: No

10. Are you concerned with DKA and AKI in Type 1 DM for using SGLt2?

Answer: No concern re AKI, but DKA is a concern. A number of trials have been done with dapagliflozin and sotiglaflozin. However, the risks of diabetic ketoacidosis remain much higher, hence only highly selected persons, with close follow up should be considered for this. It is important to note the FDA has NOT approved SGLT2i for persons with type 1 DM, but the EMA has approved these agents for Type 1 DM.