Title: HFA 23: Dapagliflozin and Peripheral Arterial Disease in Heart Failure
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Date: 24th May 2023

Dr Jawad Haider Butt

"My name is Jawad Butt. I'm a medical doctor at the Department of Cardiology, Copenhagen University Hospital, Rigshospitalet in Denmark.

What is the importance of this trial?

So, this study is important for several reasons. First, we know that patients with heart failure and PAD, that is, peripheral artery disease, that these patients have a significantly worse prognosis than patients with heart failure without PAD. In other words, patients with heart failure and PAD are a very high-risk population. Therefore, we need effective therapies to reduce the risk of heart failure, hospitalization, and cardiovascular death in these patients. In addition, we know that with certain SGLT2 inhibitors, and that is with the canagliflozin, that it increases the risk of amputations in patients with type two diabetes at high cardiovascular risk. At least that's what we saw in the chemist trials. However, this finding has not been replicated in other populations or with other SGLT2 inhibitors. And therefore, it is important to also examine whether this holds true in a heart failure population. This is interesting because patients with heart failure, all of them at least receive most of them, at least, receive diuretics. And we know that diuretics are also associated with an increased risk of amputations.

What was the patient cohort and study design?

So, this was a patient-level meta-analysis of the DAPA-HF and DELIVER trials. So, both trials enrolled patients with heart failure, that is, patients who were symptomatic, who had a NYHA class two to four, and these patients had to have a high or elevated NT-proBNP level. So, the principal difference between these two trials were that in DAPA HF, patients were enrolled if they had a reduced ejection fraction, but in DELIVER, patients were enrolled if they had a mildly reduced or a preserved ejection fraction. So,

this is a trial, or these two trials covers the entire spectrum of patients with heart failure. The study designed both trials were phase three randomized clinical trials and both randomized patients either to the SGLT2 inhibitor dapagliflozin or placebo. And the primary outcome in both trials was composite of worsening heart failure or cardiovascular death.

What is the data presented at HFA 23?

So, the data that I've presented here shows quite a few things. First, we now know that dapagliflozin is effective in reducing the primary outcome, that is, the composite of worsening heart failure and cardiovascular death, as well as each of the components of the primary outcome. And all-cause death and total heart failure hospitalizations compared with placebo. And this beneficial effect is not modified by PAD status, that is that the beneficial effect is seen in both patients with and without PAD. And the second, and probably more interesting finding is that the risk of amputations is not increased with Dapagliflozin treatment as compared with placebo. Importantly, this was the case in both patients with and without PAD.

How should these findings be put into clinical practice?

So, the take-home message of this? Well, I think there are two take-home messages. First, we know that patients with Pad are high-risk population. So, we now know that, well, dapagliflozin is an effective treatment in these patients, which means that they have a higher absolute risk reduction. So that's the first main thing. So, it's an effective therapy. And the second take-home message is that dapagliflozin is a safe therapy, especially when it comes to the risk of amputations.

What are the next steps?

So, the next steps of this, I think, is so now we have established in several publications that dapagliflozin is a safe and an effective treatment in patients with heart failure across the entire spectrum. So, the next step, I think, is that now it’s time to implement the treatment in the clinic.”