Title: HFA 23: DAPA MODA: Dapagliflozin & Cardiac Remodelling in Chronic HF
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What is known about SGLT2i's mechanism of action, and what is the importance of this study?

"We know well the benefits, the clinical benefits of SGLT2 inhibitors. However, the mechanisms underlying these clinical benefits are not very clear. We know about congestive actions and the metabolic effects on anti-inflammatory effects, but the effect on heart remodelling. Adverse heart remodelling is not well known with scarce of results and different results. So now we look at the heart to know in which way the initiation of dapagliflozin, in this case, is associated with an improvement in reverse remodelling in heart failure patients.

What is the study design, methodology and outcome measures?

Now, SGLT2 inhibitors currently are in clinical practice. So, the design of this study was open-label and singular. But one of the strengths of the design is that we recruited a chronic heart failure population with long standing heart failure and a very well optimised treatment in a clinically stable condition. The high rates of guideline-directed medical therapists were really assuring about this optimised treatment because patients were not receiving SGLT2 inhibitors, of course. So, with this inclusion criteria we recruited 162patients we intended to have, using a parallel inclusion to have similar proportion of patients with reduced ejection fraction and preserved ejection fraction. So, after the procedures of the study were directed to study remodelling, actual remodelling and left ventricular remodelling. And we included echocardiography and blood sampling at baseline just before the initiation of dapagliflozin the same day or 24 hours before. And we repeated the procedures at30 days and six months. So, another strength of the study is that the interpretation of echo parameters was blinded to the patient and to time. So, it was performed in echo core lab of the study. So, this is the way to assure that the

primary endpoint change, the primary endpoint was changing the left atrium. The ability to reverse left atrial remodelling in terms of left atrial maximal volume was reliable for us.

What are the key findings?

The key findings are the - the primary endpoint was the change in let atrial maximal volume index at the change from baseline to six months. It was positive. We observed a reduction of left atrial volume index. The reduction was mainly explained because the reduction of the reservoir volume, no other change we were observed in terms of left atrial remodelling. But it is true that we observed advanced left atrial disease in this population. So probably this explained why we didn't observe an improvement in other parameters like strain, reservoir, conduction, and contraction parameters. In addition, we observed an improvement in all parameters of left ventricular remodelling, left ventricular mass, diameters, volumes, and a mild increase in left ventricular ejection fraction and lower longitudinal strain. And it was also associated with reduction of NT proBNP levels and an improvement in quality of life. So, the main finding is that global adversary modelling was reversed by the administration of dapagliflozin in this chronic stable population.

What are the take-home messages?

So, I think in clinical practice for the clinician this study we are sure about the benefit of dapagliflozin in our patients when we need to avoid inertia of not changing patients changing treatment because we are talking about a stable population, chronic population, and the inertia usually isa problem to change treatment. So even in this population stable chronic the introduction of dapagliflozin was associated with an improvement in clinical endpoints but especially in heart health because global remodelling atrial remodelling, left ventricular remodelling, global remodelling is a very good indicator of global health of the heart. It is preventing or protecting the heart from new events from the progression of the disease in the mid and long-term follow-up.

How do the effects of dapagliflozin compare with other available treatments?

In the recent ESC guidelines, I think one of the news in these guidelines was to give us a new concept, it's left atrial disease. I think in the next years we must keep in mind the left atrium because prior trials have not addressed this question. Sacubitril/Valsartan has good data from PROVE-HF, from the evaluate trial and from PARAMOUNT in preserved ejection fraction about the ability to reduce left atrial volume and to improve to reverse left atrial remodelling. But we have no doubt about the other pillars of our treatment. But I think it's important to demonstrate that protecting left atrium we are also protecting the left ventricle and global heart function. Indeed, we are preventing the progression of the disease.

How do the effects of dapagliflozin compare with other available treatments?

There are studies demonstrating that very well that there is an association between left atrial volume and the incidence of atrial fibrillation. In our study almost half of patients were having atrial fibrillation. So, we have not looked at the incidence of new-onset atrial fibrillation. But I think atrial fibrillation is one element in one other part of the story of atrial, left atrium. So, we need to protect the remodelling, the best remodelling and this is the way to give an additional value to our treatments in this way. To prevent atrial fibrillation is one endpoint in the follow-up. But before atrial fibrillation we have left atrial disease. So, we need to keep in mind to treat early to improve health and prevent atrial fibrillation in the long-term follow-up."