ACC 22: Results From the PACIFIC AF Trial

- Hi, my name is Manesh Patel. I'm the Chief of Cardiology and Co-direct the Heart Centre at Duke University and I'm an investigator at the Duke Clinical Research Institute.

Background to the study

You know, we have patients with atrial fibrillation and we've had advances in the anticoagulation of our patients. We've gone from warfarin to DOACs or direct acting oral anticoagulants, such as a apixaban or rivaroxaban, but we still have patients with unacceptable bleeding and a lot of patients who don't get therapy. So, the background to this study is, are there new therapies that we could use in patients like that?
And asundexian is a new small molecule that inhibits factor XI, and it was studied in PACIFIC-AF.

Study design

PACIFIC-AF is a phase two study. And it's looking at understanding the dosing of asundexian, a small molecule that inhibits factor XI and is minimally lurinally cleared.
We used 20 milligrammes and 50 milligrammes once daily of asundexian and compared it to apixaban with standard dosing in 750 patients with atrial fibrillation. We followed them for about three months to see what the rates of bleeding were. The reason we're looking at bleeding is to understand the dosing relationship with asundexian and apixaban for bleeding, as we get ready to do a large phase three outcome study.

Key findings

It's important to recognise a lot of ways can be evaluated to see how patients bleed. And this was done during the COVID time, the patients were patients with atrial fibrillation and a CHA2DS2-VASc Score of about four. Many of them had some renal dysfunction, many comorbidities, heart failure, diabetes.
There were 48 total bleeding events. And even though ISTH major and non-clinically, non-major clinically relevant bleeding was the primary safety evaluation. And what we found is both doses of asundexian had less bleeding than apixaban, about 50% less.
Small numbers, but at least encouraging to show us that there is, seems to be a safety profile for the therapy.

Impact on Clinical Practice

Currently, I don't think these findings can affect clinical practice because the therapy is still being evaluated. PACIFIC-AF is one of three studies.
There's an AMI study and a stroke study. And through that, we'll learn about the dosing of the drug as we get ready for large phase three studies together. So these phase two studies will help us. What's important though, is that we want to engage patients. So we are doing something called PEARL AF, people can go to AFibopportunities.com and later this Spring, participate and tell us what matters for them if they have atrial fibrillation. Are they interested being in the study? We hope that these types of trials and agents will tell us in the future how to get to a better place for our patients with atrial fibrillation.

Next steps

Yeah, the critical next step is to actually design phase three or outcome studies that engage more people, more women, more underrepresented patients, more patients from around the world that previously have not been in trials, and hopefully develop ways in which these therapies work across those broad populations to increase the adoption of new therapies.

Take-home messages

I think we all know that many patients with atrial fibrillation have a risk of stroke and systemic embolism. Currently clinically, we don't treat them because of the bleeding risk. The take-home message of this is factor XI assay has shown us that asundexian inhibits 90% of factor XI activity. And at that rate, we have, looks like 40 to 50% of the bleeding of apixaban. So encouraging for the phase three data.