Title: ARAMIS: Anakinra versus Placebo in Acute Myocarditis
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Dr Julian Gillmore

"So my name is Julian Gillmore and I work at the National Amyloidosis Centre at University College London, and I'm going to present the results of the ATTRibute-CM trial, which is a trial of acoramidis in patients with ATTR amyloid cardiomyopathy transtherytin ATTR amyloid.

Unmet Needs of Patients and Currently Available Treatments for ATTR

Cardiomyopathy is a progressive and fatal disease. The current treatments, or the approved current treatment, consists of tafamidis, which is a small molecule drug that stabilises the TTR protein and has been shown to reduce mortality and cardiovascular hospitalizations and slow the decline of functional assessments in patients.

So really, that's the only disease-modifying therapy that is available. And one of the problems with tafamidis is it's available in some countries across the world, but the availability is not throughout the world.

Mechanism of Action of the Study Drug

So the study drug was acoromidis, and acoromidis is also like tafamidis a small molecule stabiliser of the TTR protein. So the mechanism of action is relatively similar to tafamidis, although acoromidis, the new drug, is based on a known TTR variant which has been shown to protect patients from developing this disease.

Study Design, Patient Population and Outcome Measures

So this was a randomised, double-blind, placebo-controlled trial of 30 months treatment duration. The patient population were patients with ATTR amyloid cardiomyopathy diagnosed either by a heart biopsy or what we call noninvasively and NYHA class one

to three heart failure. 632 patients were randomised two to one acoromidis to placebo, and tafamidis was permitted. The use of open-label tafamidis was permitted, but only after twelve months, and that was dependent on local availability and at the discretion of the investigator.

The primary endpoint was a hierarchical evaluation using the Finklestein Schoenfeld method of all-cause mortality, cardiovascular hospitalizations, change in NTproBNP from baseline, and change in six-minute walk distance.

Key Results

The study met its primary endpoint with a highly statistically significant p-value of less than zero. One. Importantly, 58% of the win ratio ties were broken by the first two components of the primary endpoint, so all-cause mortality and cardiovascular hospitalizations, and a separate analysis using those two components of the primary endpoint alone was statistically significant, and the results were consistent across subgroups, with the point estimates consistently. If you like, favoring acoromidis over placebo and the confidence intervals to the right of unity, if you like. So favoring acoramidis.

Safety Events

No safety concerns at all. The treatment emergent adverse events were well balanced between the two arms and actually, with respect to treatment emergent serious adverse events favored acoromidis.

Take-Home Messages

I think the main take-home message is that we now have a second effective drug to treat this condition and it's going to be very exciting to be able to treat patients with another drug that has been shown to be effective.

Next Steps

I think there's still room for improvement in terms of the treatment of this condition and there is a lot of research focusing on drugs to accelerate the removal of existing amyloid. What acoromidis and tafamidis, what those drugs do is they slow ongoing formation of amyloid, but there's a lot of focus on drugs to accelerate the removal. So I think that's probably the future."