

New mineralocorticoid receptor antagonist for heart failure

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In heart failure patients with diabetes and/or chronic kidney disease, a new, non-steroidal mineralocorticoid receptor antagonist (MRA) called finerenone was no more effective than the currently approved MRA eplerenone in reducing the heart failure biomarker N-terminal pro-B-type natriuretic peptide [NT-proBNP].

But results of the ARTS-HF trial, presented today at ESC Congress 2015, suggest that "finerenone may offer more pronounced end-organ protection than eplerenone," said Gerasimos Filippatos, MD, the study's principal investigator.

"While finerenone was not superior for the primary outcome of our study, it was more effective than eplerenone for the secondary composite endpoint of death from any cause, cardiovascular hospitalisations, or emergency presentations for worsening heart failure," said Professor Filippatos, from Athens University Hospital Attikon in Athens, Greece.

"We were somewhat surprised by this striking reduction in CV events , especially mortality in the finerenone 10-20 mg group, which appears to be the optimal dose," he said. "Preclinical studies have shown that finerenone provides greater cardiac protection and has different binding to the receptor than eplerenone and this could be the mechanism for more pronounced organ protection that could explain better outcome. If confirmed in further, adequately powered, large scale prospective, randomized studies, this could have important public health and health

cost implications."

ARTS-HF, which stands for (mineralocorticoid Receptor antagonist Tolerability Study-Heart Failure) included 1,055 patients, mean age 71 years, who presented to the emergency department with worsening heart failure and type 2 diabetes mellitus (T2DM), and/or [chronic kidney disease](#) (CKD).

Patients were randomised into six groups, one group receiving eplerenone, and the other five groups receiving different doses of finerenone for 90 days.

The primary endpoint was the percentage of individuals with more than a 30% decrease in plasma NT-proBNP from baseline to day 90, with a composite clinical secondary endpoint of death from any cause, cardiovascular (CV) hospitalisations, or emergency presentation for worsening chronic [heart failure](#). Changes in health related quality of life (QOL) were also measured.

Dosing of all medications was up-titrated through the study period. The eplerenone group started with a dose of 25 mg every other day, increasing to 25 mg daily on Day 30, with up-titration to 50 mg daily by Day 60.

The finerenone groups started with 2.5 mg, 5 mg, 7.5 mg, 10 mg or 15 mg daily, 5mg, 10mg, 15mg, 20mg and 20 mg respectively on Day 30, provided that blood potassium remained at or below 5.0 mmol/L.

By Day 90, a similar percentage of patients in each group had achieved the primary endpoint of more than a 30% decrease in plasma NT-proBNP (37.2% in the eplerenone arm compared to and 30.9%, 32.5%, 37.3%, 38.8% and 34.2% in each of the finerenone dose groups).

The secondary composite clinical endpoint occurred less frequently in all patients treated with finerenone (except for the lowest dose) compared with the eplerenone-treated patients, with the greatest risk reduction in the finerenone-treated patients who started at 10 [mg daily](#) (HR 0.56; nominal P= 0.0157).

Individual secondary endpoints were also decreased in the finerenone compared to eplerenone groups, including of CV hospitalization (HR 0.56; P= 0.0229), all-cause death (P= 0.0262) and CV death (P=0.0108) and patient-reported QOL was also consistently better with finerenone at starting doses of 7.5 and 10mg daily compared with the eplerenone group .

Adverse events, including those leading to study drug discontinuation, were similar between both groups, and postassium elevations of 5.6 mmol/L or more occurred at equal rates in both groups (4.3%).

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