Antiparasitics for Chagas cardiomyopathy

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A 40 to 80 day treatment with the antiparasitic medication benznidazole significantly reduced parasite activity in the blood, but not the progression of serious heart problems over a 5-year period among patients with established Chagas disease (CD) cardiomyopathy, results of the BENEFIT trial show.

The findings, presented at ESC Congress 2015 today, and published simultaneously online in the *New England Journal of Medicine*, "may seem disappointing but have the potential to dramatically change the way we investigate and treat CD going forward," noted the study's co-principal investigator Carlos Morillo MD, from The Population Health Research Institute at Hamilton Health Sciences, McMaster University in Hamilton, Ontario, Canada.

"We confirmed that benznidazole has significant antiparasitic activity but there was no clear reduction in clinical outcomes," he explained.

"Recent data indicate that parasite persistence may play a pivotal role in the pathogenesis of chronic Chagas cardiomyopathy, but until now we did not know whether antiparasitic treatment could prevent its deterioration over time. Our results confirm that with the current treatment, significant reductions in parasite DNA detection can be achieved. The lack of benefit in reducing the progression of cardiomyopathy may have been related to strain susceptibility or insufficient long-term activity against the parasite, or to the fact that the disease had already progressed to an irreversible state," he added.

BENEFIT (which stands for BENznidazole Evaluation For Interrupting Trypanosomiasis Trial) included 2,854 patients from 5 countries in Central and South America.

It is the largest study in Chagas disease and the most comprehensive program ever conducted and will inform research into the field for some time to come" said Jose Antonio Marin-Neto, MD, co-principal investigator of the study, from the University of Sao Paulo, in Riberao Preto, Brazil.

All patients had serologic evidence of the Trypanosoma cruzi parasite which causes Chagas, as well as electrocardiographic and other typical cardiac abnormalities characteristic of Chagas cardiomyopathy (CCM).

"The T-cruzi parasite is transmitted to humans by triatominae insects and is curable when treated early with antiparasitics. However, it is often not recognised at this stage and 30% - 40% of chronic infections lead to cardiomyopathy within 10-30 years," explained Dr. Morillo.

The patients were randomised to treatment with placebo or benznidazole for 40 - 80 days, with the primary outcome of the study being a composite of all cause death, resuscitated cardiac arrest, sustained ventricular tachycardia, insertion of pacemaker or cardiac defibrillator, cardiac transplantation, development of new heart failure, and stroke, or systemic or pulmonary thromboembolic events.

After an average follow-up of 5.4 years, the primary outcome occurred in a similar percentage of patients in the treatment and placebo arms (27.5% and 29.1% respectively; hazard ratio [HR] 0.93; 95% confidence interval [CI] 0.81-1.07; P=0.31).

Blood parasite detection by polymerase chain reaction was significantly reduced after treatment, compared to placebo (66.2% versus 33.5%), but this effect, although still significant, was diminished after 5 years (46.7% versus 33.1% respectively (all P