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Abstract

Letter to the Editor, comment on article entitled "Risk Factors for Heart Failure in Patients With Type 2 Diabetes Mellitus and Stage 4 Chronic Kidney Disease Treated With Bardoxolone Methyl" by Chin et al in the Journal of Cardiac Failure.

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Comment on: Risk Factors for Heart Failure in Patients with Type 2 Diabetes Mellitus and Stage 4 Chronic Kidney Disease Treated with Bardoxolone Methyl

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Comment on: Risk Factors for Heart Failure in Patients with Type 2 Diabetes Mellitus and Stage 4 Chronic Kidney Disease Treated with Bardoxolone Methyl

To the Editor:

We read with great interest the article entitled, “Risk factors for Heart Failure in Patients with Type 2 Diabetes Mellitus and Stage 4 Chronic Kidney Disease Treated with Bardoxolone Methyl” by Chin et al [1] in a recent issue of *Journal of Cardiac Failure*. The authors reported that patients treated with bardoxolone methyl in the BEACON Phase III human clinical trial with a baseline B-type natriuretic peptide (BNP) ≥ 200 pg/ml or prior hospitalisation had a 60% increased risk of heart failure compared to the placebo group. We believe that this information is crucial in order to design successful human clinical trials investigating the potential benefits of bardoxolone methyl in the future. However, we have some additional comments regarding the outcome of the study.

Firstly, the baseline BNP data in the classification trees for a) Figure 1: Classification tree for heart failure events in BEACON and b) Figure 2: Classification tree for fluid overload or heart failure events are set to a different level for the bardoxolone methyl group compared to the control group (bardoxolone methyl = ± 183 .pg/ml, placebo= ± 229.5 pg/ml). Furthermore, a study by Wang et al., reported that BNP levels as low as 20 pg/ml can increase the risk of heart failure [2]. In addition, the conventional values for diagnosis of heart failure are usually between 80 and 100 pg/ml [3, 4]. Therefore, an equal comparison between baseline BNP levels and both the bardoxolone methyl and placebo group in the BEACON clinical trial is necessary. A consideration of the risk of heart failure in patients treated with bardoxolone methyl compared to placebo with lower BNP levels would also be interesting to consider in future studies.

Secondly, there is controversy surrounding the usefulness of BNP as a biomarker for heart failure mechanisms, since levels vary widely in the general population based on factors including age, gender and BMI [5, 6]. Specifically, elevated BNP levels can occur in conditions independent of heart failure including old age, the use of hormone replacement therapy, and obesity [7]. In this study, patients had type 2 diabetes and stage 4 chronic kidney disease and were divided only into a bardoxolone methyl treatment or placebo group, and were not divided according to other parameters such as age, gender and BMI. Therefore, whether there were differences between these factors in the BEACON trial may also be interesting parameters to investigate to eliminate potential non heart failure mechanisms that have the ability to elevate BNP levels.

In conclusion, despite the risk factors for heart failure identified in this study, the benefits of bardoxolone methyl in earlier human clinical trials and preclinical animal studies cannot be ignored [8]. Future studies should focus on identifying molecular mechanisms in the heart and the cardiovascular network that explain potential increased risks of the development of heart failure in patients treated with bardoxolone methyl [9]. This will allow the development of more robust human clinical trials using bardoxolone methyl in the future.

Disclosure

The authors have nothing to disclose.

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