

[LETTERS TO THE EDITOR]

Reply to “The Effects of Tranilast on Cardiomyopathy in Becker Muscular Dystrophy Requires Profound Cardiac and Neurologic Evaluations”

Key words: muscular dystrophy, cardiomyopathy, cardioprotective therapy, tranilast, transient receptor potential cation channel, subfamily V, member 2 (TRPV2)

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The Authors Reply We appreciate the thorough comments by Stöllberger et al. on our paper regarding the pilot study of tranilast for cardiomyopathy of muscular dystrophy (1). Although tranilast has been approved for allergic diseases, this pilot study was the first-in-human trial for heart failure and was thus planned as a short pre-study for a subsequent multi-center trial. Both participants were patients with muscular dystrophy and advanced heart failure. Patient 2 was diagnosed on the basis of dystrophic features in a muscle biopsy, but immunological studies were not available at the time, and no mutations in dystrophin were detected. We are still trying to reach a definitive diagnosis for this patient. Next-generation sequencing detected a heterozygous novel mutation in *SYNE1* (c.18137C>T, p.Thr6046Met). His sister, who has complete atrioventricular block and arrhythmia (supraventricular premature beats, ventricular premature beats and non-sustained ventricular tachycardia) and is receiving beta-blocker without skeletal muscle involvement, has the same mutation (Fig. 1). These facts strongly suggest Emery-Dreifuss muscular dystrophy 4 (2) in Patient 2, but we can-

not yet confirm this.

Patients with muscular dystrophy frequently have low blood pressure, and the systolic blood pressure in both patients was around 80 mmHg. For this reason, we did not up-titrate the enalapril dosage. No significant changes to the electrocardiogram findings were seen during the study period (Fig. 2). As mentioned in the text of the original paper (3), the heart rate and ventricular premature beats were increased in Patient 1, but atrial fibrillation was not observed in either patient. As shown in the supplementary materials of the original paper (3), the number of eosinophils was below 700/ μ L in both patients during the study period, and neither leucopenia nor thrombocytopenia was found. The hepatic function deteriorated transiently in Patient 2 during the administration of antibiotics but recovered soon after stopping antibiotics. We therefore did not consider this event to be related to tranilast (3).

Both patients developed slowly progressive muscle weakness and respiratory dysfunction, and no neurological improvements were observed after starting treatment. In addition, no obvious changes in the creatine kinase levels were noted. Although tranilast can be effective on skeletal muscle in muscular dystrophy, milder cases should be selected to assess the effects on skeletal muscle.

The pharmacological effects of tranilast on cardiomyocytes are not specific for patients with muscular dystrophy. After confirming the effects of tranilast in the next multi-center study for cardiomyopathy in muscular dystrophy, we hope to collaborate with cardiovascular specialists to develop a study on heart failure in the general population.

The authors state that they have no Conflict of Interest (COI).

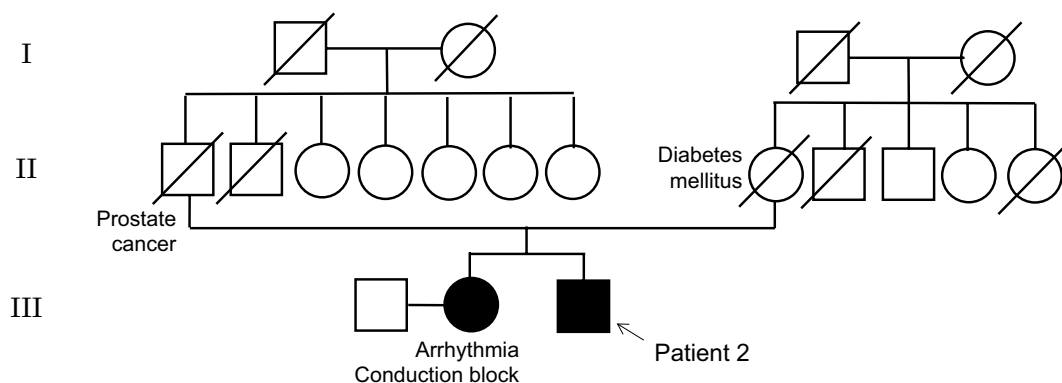


Figure 1. The pedigree of Patient 2.

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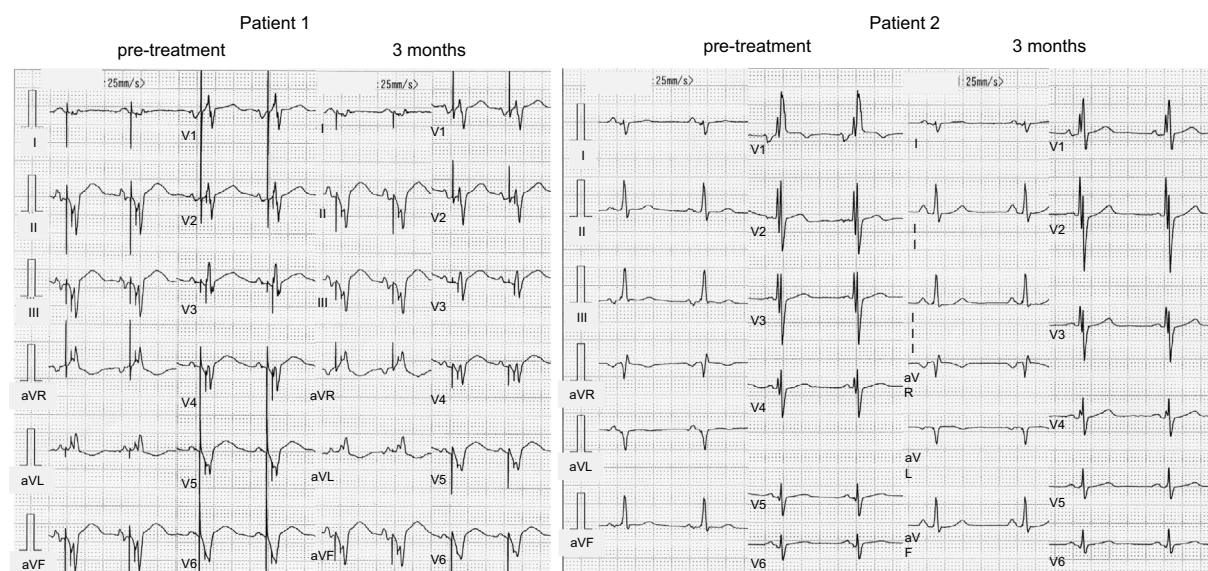


Figure 2. Electrocardiograms before and after treatment.

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