Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Nebivolol Treatment in Pediatric Heart Failure Patients

Category

Therapeutic – New Method of Treatment

Problem

Pathophysiology of pediatric heart failure is vastly different than in adults and difficult to treat, requiring specific and unique treatments.

Technology Overview

CU investigators have demonstrated a beta-blocker with high specificity towards the beta-1 receptor may be used in treatment of pediatric heart failure

IP Status

- Patent Issued in US
- Available for Exclusive or Non-Exclusive Licensing

Value Proposition

- Straightforward treatment for pediatric heart disease
- Pathway specificity to beta-1 receptor

Market Attractions

- Beta-blocker market valued at $1.2B
- Nebivolol generated ~ $300M globally in 2016
- Breakthrough treatment for pediatric heart failure

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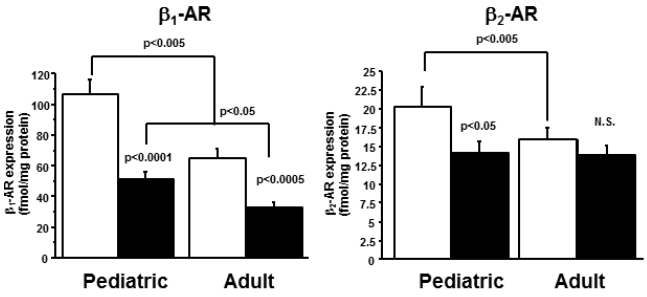
Problem: Heart failure is one of the leading causes of death in the world, however the pathophysiology of the development of myocardial dysfunction and heart failure in children is poorly understood. For example, the reproducible clinical benefits of beta-blockers in adults have not provided the same clinical success in children with heart failure. Due to the lack of clinical benefit in children seen with carvediol, it is hypothesized that children have critical differences in beta-adrenergic receptor remodeling in response to heart failure than in adults. From a therapeutic standpoint, these characteristics indicate that it is likely children with heart failure represent a population with unique needs and provide an opportunity for the development of novel therapeutics or new indications for existing therapeutic modalities.

Technical Solution and Key Value Propositions:

A team at the University of Colorado led by Dr. Brian Stauffer discovered that the beta-blocker nebivolol may be used as a treatment for children suffering from heart failure. Nebivolol has greater than 400 times more affinity for the beta-1 receptor than beta-2. Beta-2 activation is more beneficial by protecting against cellular apoptosis and providing the secondary messenger for muscle contraction function. Since downregulation of beta-2 receptor is shown in children with heart failure, it would be important to selectively block the beta-1 receptor while leaving the useful beta-2 receptor active in children. This efficacy is at least twice as beta-1 selective as the current beta-blocker used, metoprolol. Nebivolol provides the best subtype specific profile of all beta blockers to treat heart failure in pediatric patients.



(Left): Expression of beta receptors in non-failing and failing pediatric and adult hearts. Both beta-1 and beta-2 receptors are downregulated in children while beta-2 expression is maintained in adults.

Development Status:

Currently used to treat heart failure in Europe, but not FDA-approved in the United States. There is no indication of nebivolol being used to treat pediatric patients with heart disease.

Key Documents and Sources:

- Miaymoto SD, Stauffer BL, Nakono S, et al. Beta-adrenergic adaptation in paediatric idiopathic dilated cardiomyopathy. Eur Heart J. 2014 Jan;35(1):33-41.
- Shaddy RE, Boucek MM, Hsu DT, et al. Carvedilol for children and adolescents with heart failure: a randomized controlled trial. JAMA. 2007;298(10):1171-9.
- US 9,456,997B2: "Selective Inhibition of beta1-Adrenergic Receptors for the Treatment of Pediatric Heart Failure"