Cleveland Clinic Innovations

PRODUCT
Beta-1 adrenergic receptor autoantibodies.

INDICATION
Therapeutic, AntiBody (Ab) / NanoBody, Cardiovascular.

VALUE PROPOSITION
- Increased benefit and clinical outcomes for patients on β-blockers.
- Specific modulation and targeting that does not alter β2AR signaling.
- Potential benefits for heart failure patients while preventing cardiac deterioration.

DEVELOPMENT STAGE
Product development and scoping.

INTELLECTUAL PROPERTY
PCT# US2022014951

RELATED PUBLICATIONS
Tang, W. H. W., & Naga Prasad, S. V. (2022). Autoantibodies and Cardiomyopathy: Focus on Beta-1 Adrenergic Receptor Autoantibodies. Journal of Cardiovascular Pharmacology, 80(3), 354-363.

CONTACT INFORMATION
Joe Barone
Director, Innovation Sales & Partnership
baronej2@ccf.org
216.399.2999
IDF 2021-009

Beta-1 Adrenergic Receptor Autoantibodies as Cardiovascular Therapeutics

Inventors: W.H. Wilson Tang, MD, Sathyamangla v. Naga Prasad, PhD, Maradumane Mohan
Cardiovascular Medicine, Heart, Vascular, & Thoracic Institute

UNMET NEED

Circulating autoantibodies may be critically linked to heart failure pathogenesis. β-blockers, which offer a significant line of therapy for heart disease, are thought to provide beneficial outcomes by impeding the βAR signals from sympathetic overdrive. However, their role in the upregulation of β1AR may underlie worsening outcomes of heart failure due to binding by β1AR autoantibodies that may prolong the signal. Significant myocardial recovery in response to β-blocker treatment has been demonstrated in patients harboring β1AR autoantibodies belonging to the IgG3 subclass.

SOLUTION

Patients characterized by the presence of IgG3(+) β1AR autoantibodies responded better to β-blocker treatment compared to their counterparts. The use of the IgG3(+) β1AR autoantibodies may provide unique regulation of these pathways, potentially leading to benefits for heart failure patients while preventing cardiac deterioration.

a) IgG3(+) β1AR autoantibodies provide beneficial composite end-point clinical outcomes in patients who are on β-blockers.

b) IgG3(+) β1AR autoantibodies specifically modulate only β1AR agonist or antagonist targets and do not alter β2AR signaling.

c) Presence of IgG3(+) β1AR autoantibodies impairs classical G-protein coupling and promotes beneficial β-arrestin dependent pathways.

d) IgG3(+) β1AR autoantibodies promote preferential coupling to G-proteins in response to selective β1AR blocker Meto.

e) IgG3(+) β1AR autoantibodies preferentially allow for G-protein coupling leading to cAMP generation resulting in a potential normalization and reduction in the heart rate, thereby playing a dynamic role in temporally regulating β1AR downstream signaling.