ORPHANET JOURNAL OF RARE DISEASES

ORAL PRESENTATION Open Access

DISCOVERY: a study examining the prevalence of transthyretin mutations in subjects suspected of having cardiac amyloidosis

Olakunle Akinboboye[1*], Karthik Ananthasubramaniam[2], Amir Malik[3], Alberta Warner[4], Verena Karsten[5], Thibaud Damy[6], Herman A Taylor[7], Mathew S Maurer[8]

From First European Congress on Hereditary ATTR amyloidosis
Paris, France. 2-3 November 2015

Background

Cardiac amyloidosis (CA) is caused by extracellular myocardial deposition of either immunoglobulin light-chain (AL) or transthyretin (ATTR) fibrils. Two forms of ATTR CA cause life-threatening cardiomyopathy: an inherited form arising from misfolding of mutated ATTR (familial amyloid cardiomyopathy [FAC]) and a sporadic form caused by wild-type ATTR (senile systemic amyloidosis [SSA]). More than half of over 100 reported ATTR mutations are associated with FAC. The most common mutation in the US is Val122Ile found in 3-4% of African Americans (AA). FAC can be difficult to recognize clinically and is likely under diagnosed. The DISCOVERY study aims to determine the prevalence of TTR mutations and FAC diagnosis in a cohort of patients (pts) with clinical features suggestive of CA.

Methods

This is a prospective, multi-center study in adults with two or more of the following eligibility criteria: heart failure signs and symptoms, intraventricular septal thickness (IVS) of >12 mm, LV diastolic dysfunction, low voltage ECG, or history of carpal tunnel disease (CTD). DNA from blood samples is used for sequencing of the TTR gene coding regions by a central lab. Assessments in pts with TTR mutations include cardiac biomarkers, echocardiogram and optional abdominal fat pat aspiration and 6-minute walk test. Descriptive statistics will be utilized.

Results

As of May 2015, 146 pts have been enrolled. At baseline, the mean (Std) age of pts is 64 (13) yrs, 61% are men and 66% are AA. A total of 14 (10%) pts had a Val122Ile mutation and 1 pt had a novel mutation Arg103His. The Gly6Ser polymorphism was found in 8 (5%) pts. The Val122Ile cohort consisted of 40% males with a mean (StD) age of 66 (16). Heart failure signs and symptoms and IVS > 12 mm was reported in 71% and 79% of Val122IIle pts respectively. The majority of pts had NYHA class II (56%) and III (22%) heart failure, 21% had low voltage ECGs and 14% had CTD.

Conclusions

These preliminary data suggest that approximately 10% of pts with clinical and/or radiologic findings suggestive of cardiac amyloidosis have a pathogenic TTR mutation which could potentially lead to a diagnosis of FAC. Additional data on clinical features and tissue diagnosis of FAC in these pts will be presented.

Authors' details
[1]Queens Heart Institute, Medicine, 11422, Rosedale, USA. [2]Henry Ford Hospital, Heart and Vascular Institute, 48202, Detroit, USA. [3]Heart Center of North Texas, Cardiology, 76104, Fort Worth, USA. [4]Los Angeles Veterans Affairs Health Care System, Echo lab and HF service, 90073, Los Angeles, USA. [5]Alnylam Pharmaceuticals, Clinical Development, 02142, Cambridge, USA. [6]APHP, Cardiology and Amyloidosis Mondor Network, 94000, Creteil, France. [7]Morehouse School of Medicine, Cardiovascular Research Institute, 30310, Atlanta, USA. [8]Columbia University Medical Center, Medicine, 10032, New Yok, USA.

Published: 2 November 2015

doi:10.1186/1750-1172-10-S1-O8
Cite this article as: Akinboboye *et al.*: DISCOVERY: a study examining the prevalence of transthyretin mutations in subjects suspected of having cardiac amyloidosis. *Orphanet Journal of Rare Diseases* 2015 **10**(Suppl 1):O8.

[1]Queens Heart Institute, Medicine, 11422, Rosedale, USA
Full list of author information is available at the end of the article

BioMed Central

© 2015 Akinboboye et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.