Phase I trial demonstrates first pharmacological treatment able to improve cardiac function in stiff-heart syndrome

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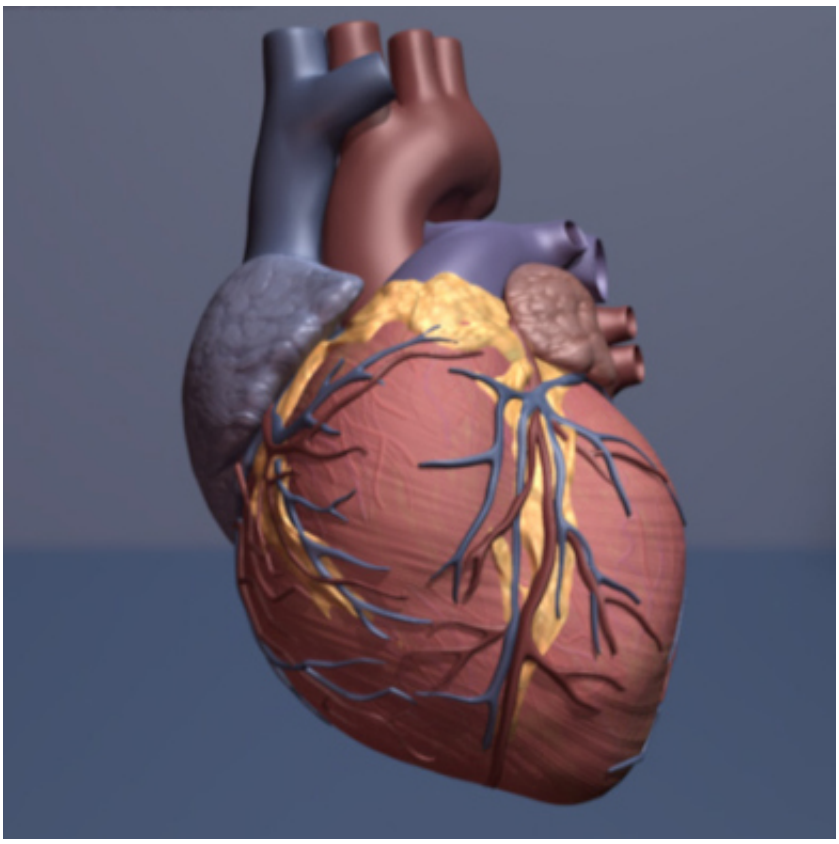

Human heart. Credit: copyright American Heart Association

Transthyretin-related cardiac amyloidosis is a progressive disease characterized by the deposition of amyloid protein fibrils in the heart. Amyloid fibril deposition thickens and stiffens the heart walls, and the

disease is also known as stiff-heart syndrome. The accumulation of amyloid fibrils causes heart failure, and patients suffer from fluid retention, fatigue, and arrhythmias. The disease can be caused by genetic mutations or related to aging. Prognosis is poor, and untreated patients survive for an average of just 3 years.

Now, the results of a study published in the *The New England Journal of Medicine* (*NEJM*) promise to radically alter the prospects of patients with this disease. The study was led by Dr. Pablo Garcia-Pavía, who heads the Inherited Cardiac Diseases Section at Hospital Universitario Puerta de Hierro and is a research scientist at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) and within the Spanish cardiovascular research network (CIBERCV).

Coinciding with the publication of the study, Dr. Pablo Garcia-Pavía has today presented the results of the first clinical trial with an amyloid-removing drug for the treatment of cardiac amyloidosis.

The study represents a major advance in the treatment of the disease. Although currently available treatments effectively prevent the accumulation of more amyloid fibrils and delay disease progression, they do not directly remove any amyloid protein already deposited in the heart.

Current treatment options include transthyretin-stabilizing therapy and measures to control associated cardiovascular complications. The only intervention currently able to restore cardiac function in this disease is heart transplantation.

The only drug approved to treat transthyretin-related cardiac amyloidosis is tafamidis, an oral transthyretin stabilizer. Tafamidis improves survival and reduces hospitalizations; however, it does not reverse disease symptoms that are already established.

The initial results of the trial, which included 40 patients in France, The Netherlands, Germany, and Spain and was coordinated by Dr. García-Pavía, show that the new drug is safe and appears to reduce the amount of amyloid protein deposited in the heart.

Developed by the Swiss company Neurimmune, the new medication is an antibody that binds to transthyretin amyloid protein. The antibody was first isolated from memory B cells obtained from healthy elderly individuals.

In the study, the antibody was used to stimulate the patients' own defense systems, resulting in the elimination of cardiac amyloid fibrils. The antibody was administered to patients intravenously in progressively increasing monthly doses over a 12-month period.

"Patients who received higher antibody doses seemed to show a greater reduction in amyloid deposits in the heart and greater improvements in a range of cardiac parameters," said Dr. García-Pavía.

The *NEJM* article concludes that the phase I proof-of-concept study demonstrates the safety of this treatment in patients and supports further clinical trials of this antibody.

More information: Pablo Garcia-Pavia et al, Phase 1 Trial of Antibody NI006 for Depletion of Cardiac Transthyretin Amyloid, *New England Journal of Medicine* (2023). DOI: 10.1056/NEJMoa2303765

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