National University Heart Centre Singapore

MEDIA RELEASE

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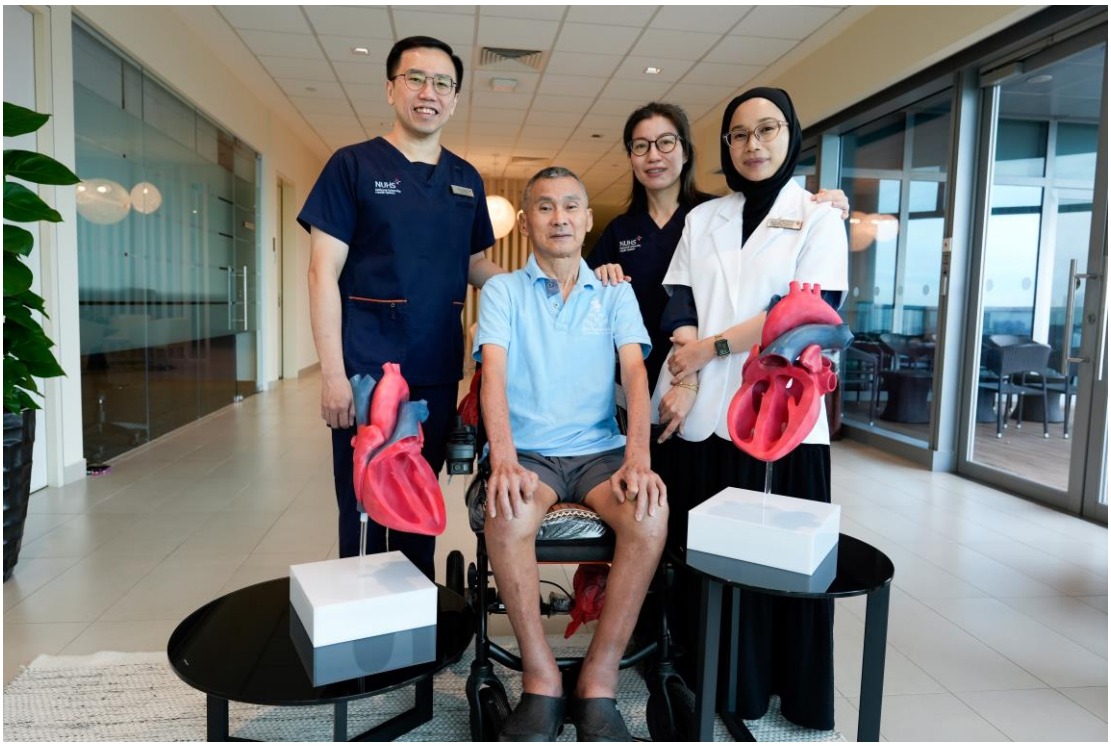
For Immediate Publication

A NEW HOPE FOR PATIENTS SUFFERING FROM POTENTIALLY FATAL RARE HEART DISEASE: NUHCS IS FIRST IN ASIA TO RECRUIT PATIENTS FOR LANDMARK GENE EDITING CLINICAL TRIAL

The international study explores gene editing therapy to stop the production of proteins causing the disease in ATTR-CM patients



From left: Asst Prof Lin Weiqin, Clinical Director of the Heart Failure and Cardiomyopathy Programme at the National University Heart Centre, Singapore (NUHCS); Mr Chua Ah Hai, who is a participant in the MAGNITUDE clinical trial; Dr Kay Ng, Senior Consultant, Division of Neurology, Department of Medicine, National University Hospital; Nur Faezah Binte Md Fadzillah, Clinical Research Coordinator, NUHCS

SINGAPORE — While receiving treatment for a car accident ten years ago, Mr Chua learnt that he had an abnormal build-up of protein in his heart vessels. This discovery led to the diagnosis of a condition known as transthyretin amyloid cardiomyopathy (ATTR-CM), a rare disease currently affecting approximately 150 patients in Singapore.

ATTR-CM is caused by the build-up of misfolded, deformed transthyretin proteins in the heart, nerves and other organs due to genetic mutation or ageing. Symptoms of this potentially fatal rare disease are often vague and may include numbness in the hands and feet, lethargy and dizziness. If not diagnosed and treated promptly, ATTR-CM can lead to heart failure.

Over time, Mr Chua's hands and legs became stiff, and the once active 62-year-old could no longer walk. The subsequent years following his diagnosis were riddled with frequent visits to the hospital due to episodes of heart failure and multiple injuries from falls resulting from nerve issues caused by the disease.

Despite being on years of medication, Mr Chua's condition had continued to decline, and his growing need for assistance with simple everyday tasks had greatly affected his spirit. There is currently no cure for this debilitating illness.

A new international clinical trial may be set to change the trajectory of this disease for patients suffering from ATTR-CM – including Mr Chua. The MAGNITUDE study involves a single-dose gene editing therapy administered intravenously that will alter the patient's DNA, slowing down the production of the abnormal protein that causes the disease.

Novel treatment offers new hope for patients

Assistant Professor Lin Weiqin, Clinical Director of the Heart Failure and Cardiomyopathy Programme at the National University Heart Centre, Singapore (NUHCS), is leading the Singapore arm of this trial. He shared that the double-blind study will investigate the impact of the gene editing research medicine Nexiguran Ziclumeran (nex-z, also known as NTLA-2001) on ATTR-CM.

"Gene editing therapy has been approved in other countries, for use in some neuro-muscular conditions, cancers and inherited blood disorders. If this trial is successful, it will be the first DNA altering treatment used in the field of adult cardiology and offers new hope to patients living with ATTR-CM," explained Asst Prof Lin, who is also a Senior Consultant at NUHCS.

In Asia, the first patient of the double-blind clinical trial was recruited in Singapore and received his infusion in September 2024 at NUHCS. Since then, four more patients have been involved in the study, including Mr Chua, who was the fifth and most recent participant. The gene editing therapy is administered alongside the standard treatment for ATTR-CM as part of the study.

While it may take another two to three years to see the outcomes of this study, early results of the trial medication in early phase clinical trials have shown promising results, with "consistent, rapid, and durable reductions" in the abnormal protein that causes ATTR-CM, and minimal side effects.[1] The patients in Singapore have also not reported any side effects thus far.

[1] Fontana M, Solomon SD, Kachadourian J, Walsh L, Rocha R, Lebwohl D, Smith D, Täubel J, Gane EJ, Pilebro B, Adams D, Razvi Y, Olbertz J, Haagensen A, Zhu P, Xu Y, Leung A, Sonderfan A, Gutstein DE, Gillmore JD. CRISPR-Cas9 Gene Editing with Nexiguran Ziclumeran for ATTR Cardiomyopathy. N Engl J Med. 2024 Dec 12;391(23):2231-2241. doi: 10.1056/NEJMoa2412309. Epub 2024 Nov 16. PMID: 39555828.

National University Heart Centre Singapore

NUHCS is the coordinating site for the Singapore trial. The heart centre is still recruiting patients, who must fulfil the following criteria:

- Between 18 to 90 years old
- Diagnosed with heart failure due to ATTR
- On medication for heart failure and have experienced heart failure in the past year
- For females, they are only eligible if they can no longer have children.

Chinese Glossary

National University Heart Centre, Singapore (NUHCS)	新加坡国立大学心脏中心 (国大心脏中心)
Assistant Professor Lin Weiqin Clinical Director, Heart Failure and Cardiomyopathy Programme National University Heart Centre, Singapore (NUHCS) Senior Consultant, Department of Cardiology National University Heart Centre, Singapore (NUHCS)	林偉勤 助理教授 心力衰竭及心肌病计划临床主任 国大心脏中心 心脏内科高级顾问医生 国大心脏中心
Transthyretin amyloid cardiomyopathy (ATTR-CM)	转甲状腺素蛋白淀粉样变性心肌病
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About the National University Heart Centre, Singapore (NUHCS)

The National University Heart Centre, Singapore (NUHCS) is an academic, national specialist centre under the National University Health System (NUHS). NUHCS brings together the resources, expertise and capabilities in the areas of Cardiology, Cardiothoracic and Vascular Surgery to better meet the needs of the growing number of patients with heart disease and raise the future generation of medical professionals.

As one of two national heart centres in Singapore for the treatment and management of complex cardiovascular diseases, NUHCS offers six core clinical programmes including Heart Failure & Cardiomyopathy, Structural Heart Disease, Acute Coronary Syndrome, Heart Rhythm, Congenital & Structural Heart Disease and Women's Heart

Health. The centre has been awarded two institutional Peaks of Excellence for its Minimally-invasive Cardiothoracic Surgery and Aortic Centre Programme, and has been ranked top in Singapore for three consecutive years in 2022, 2023 and 2024 for the specialty of Cardiac Surgery in Newsweek's "World's Best Hospital" Award.

Comprising a team of internationally-recognised cardiologists and surgeons from the cardiothoracic and vascular specialties, NUHCS serves as a referral national centre for cardiothoracic and vascular conditions and provides a comprehensive approach to the treatment of these patients. The holistic patient-care approach is backed by leading translational research at the Cardiovascular Research Institute (CVRI) and Cardiovascular Metabolic Translational Program, all of which complements these advanced quaternary clinical services to deliver state-of-the-art treatment solutions to the most challenging heart, lung and circulatory diseases.

NUHCS services span across four locations to serve the western and central locations in Singapore:

- NUHCS at National University Hospital (NUH), Kent Ridge - Main Operations
- NUHCS Heart Clinic @ Ng Teng Fong General Hospital (NTFGH)
- NUHCS Heart Clinic @ Jurong Medical Centre (JMC)
- NUHCS Heart Clinic @ Alexandra Hospital (AH)

For more information, visit: https://www.nuhcs.com.sg.