Early experience optimizing immunosuppressive use and monitoring in MyPEAK™-1, a first-in-human study of TN-201, an AAV9 gene replacement therapy in *MYBPC3*-associated hypertrophic cardiomyopathy

Milind Desai, MD MBA FACC FAHA FESC
Haslam Family Endowed Chair and Professor of Medicine, CCLCM
Vice Chair and Director HCM Center, HVTI | Cleveland Clinic
Honorary Professor, University of Oxford, UK

Sherif Nagueh, MD | Houston Methodist
John Giudicessi, MD PhD | Mayo Clinic

MyPEAK™-1

Cleveland Clinic

Heart Failure & World Congress on Acute Heart Failure 2026

Study was sponsored by Tenaya Therapeutics, Inc., South San Francisco, CA.
Disclosures: I am on the executive steering committee of NIH-sponsored HCMR trial. Study PI of trials sponsored by Bristol Myers Squibb, Edgewise, Viz AI, Cytokinetics, and Tenaya

MyPEAK-1: Phase 1b/2 trial of TN-201 in adults with *MYBPC3*-associated HCM

Study Objectives:

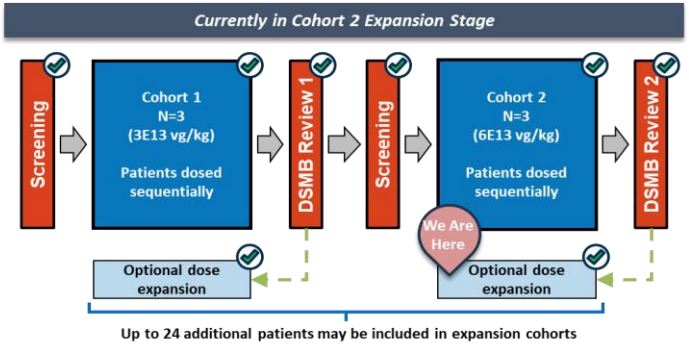
- Safety, tolerability, dose-finding, pharmacodynamics

Design:

- Open-label, dose-escalation and dose expansion
- 52-week trial with 4-year safety and efficacy follow-up

Key Eligibility Criteria:

- Age 18 to 75 with HCM, P/LP *MYBPC3* mutation, NYHA Class II or III

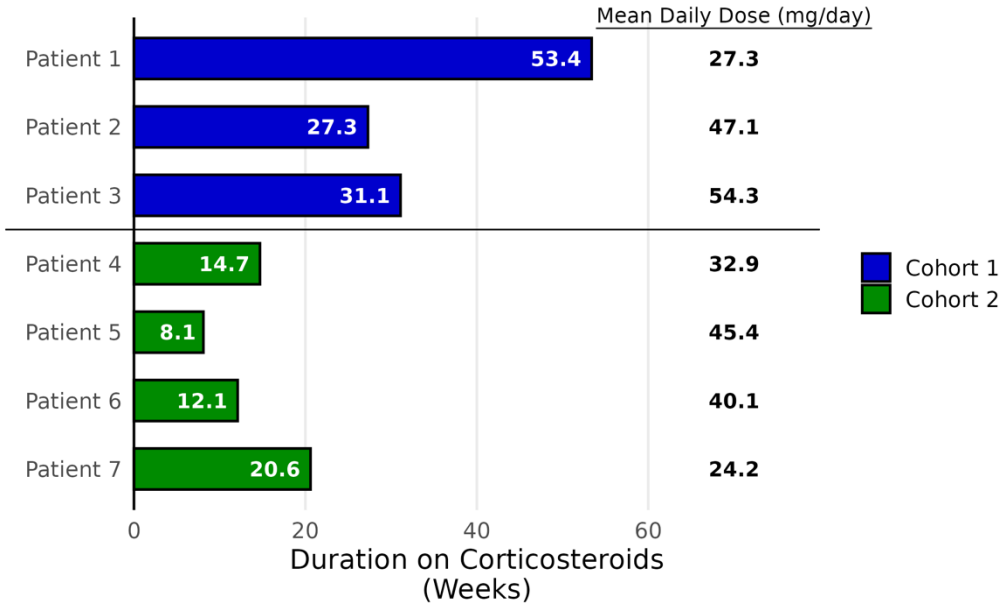


- Majority of treatment-emergent **adverse events** were **mild, transient and/or reversible**
  - Nausea (n=6) was the most common treatment-emergent adverse event
  - Two treatment-related serious adverse events (SAEs) occurred , one SAE of moderate (Grade 2) transaminase elevations, treated with IV steroid **in hospital, one SAE of mild (Grade 1) complement elevation monitored in hospital**
- **Majority** of patients (n=4) experienced **reversible asymptomatic elevations in liver enzymes**
  - Three patients in Cohort 2 experienced **laboratory abnormalities, including complement elevation, related to innate immune response** within 1 week of dosing, **resolved in days without additional treatment or organ involvement**
  - **All 7 patients have tapered off** prophylactic immunosuppression with prednisone and sirolimus
  - **No signs of cardiotoxicity**, including **no declines in left ventricular ejection fraction (LVEF)**
- Data on safety, tolerability, and immunosuppression come from **February 2026 safety data cut**

P/LP = pathogenic / likely pathogenic

Optimized immunosuppression regimen reduced steroid requirements in Cohort 2

Corticosteroid Duration and Daily Dose



IS Adjustments During Cohort 1

- Reduced maximum starting dose of prednisone dose from 80 mg to 60 mg
- Sirolimus initiated earlier (Day -7)
- Weekly monitoring during taper

Cohort 2 Results

- Despite higher dose of TN-201, Cohort 2 had fewer, lower elevations in AST/ALT
- Prednisone taper shorter for Cohort 2 (97±37 days) vs. Cohort 1 (262±98 days)

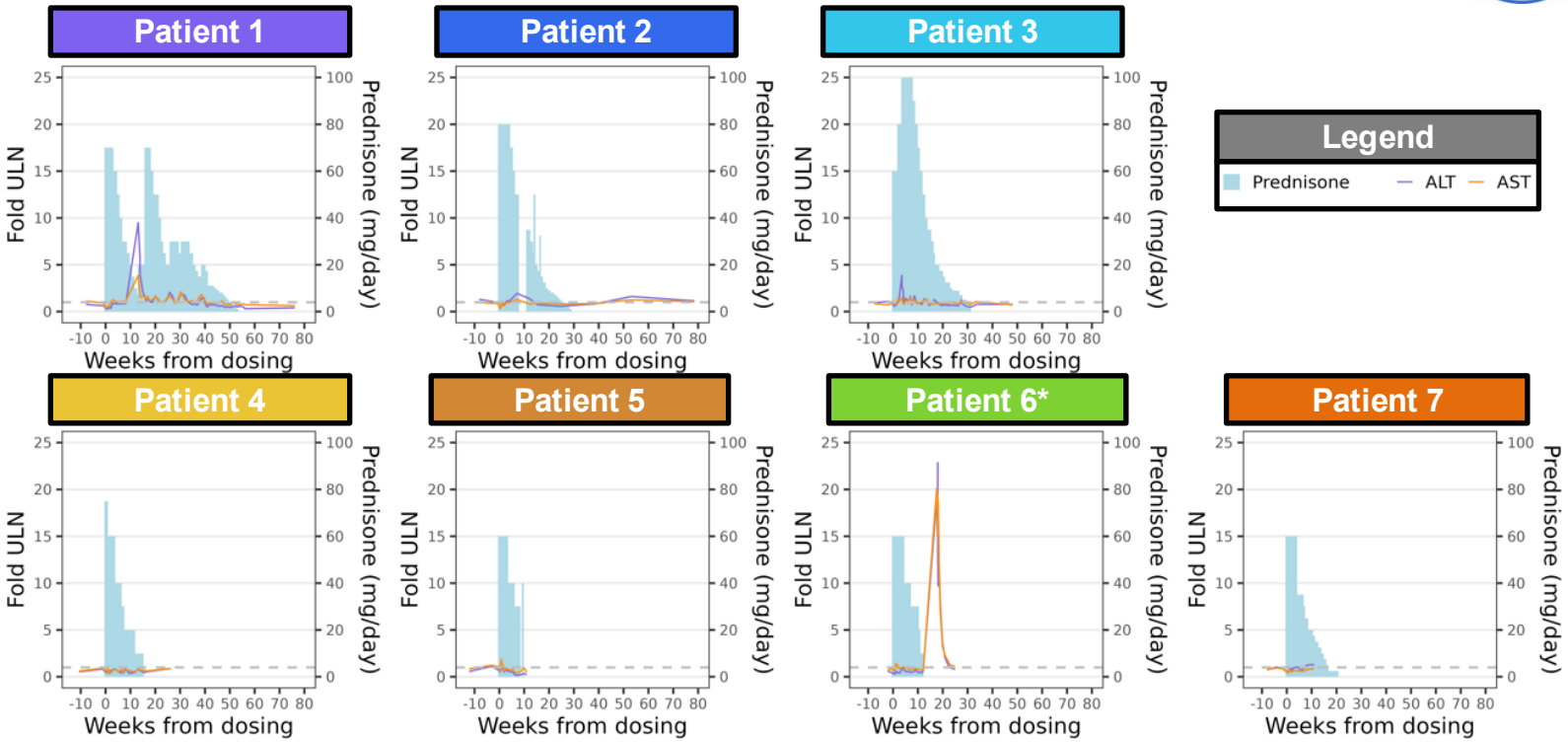
Safety data cut February 2026

IS = immunosuppression

Liver enzyme levels maintained with less prednisone

Cohort 1

Cohort 2

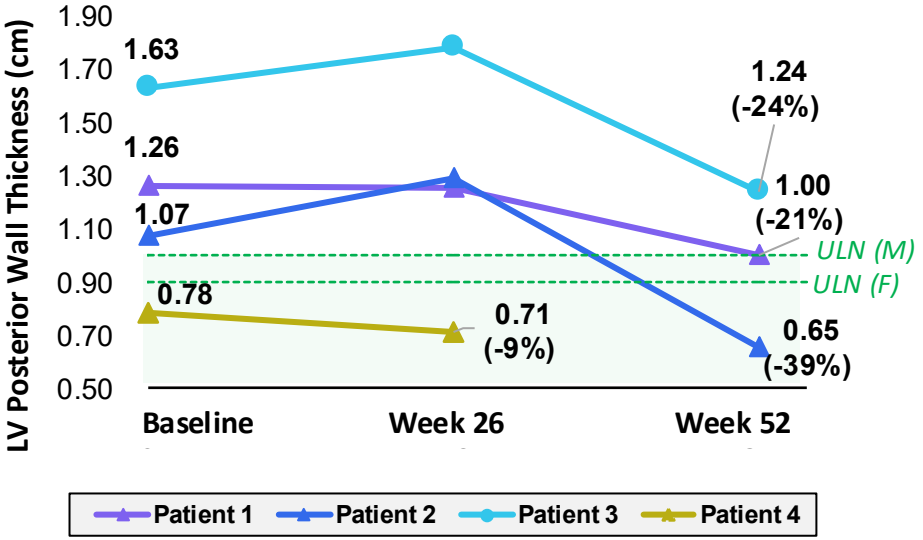


*Asymptomatic liver enzyme elevation related concomitant medication and unrelated to TN-201. Elevation resolved immediately following discontinuation of concomitant medication.

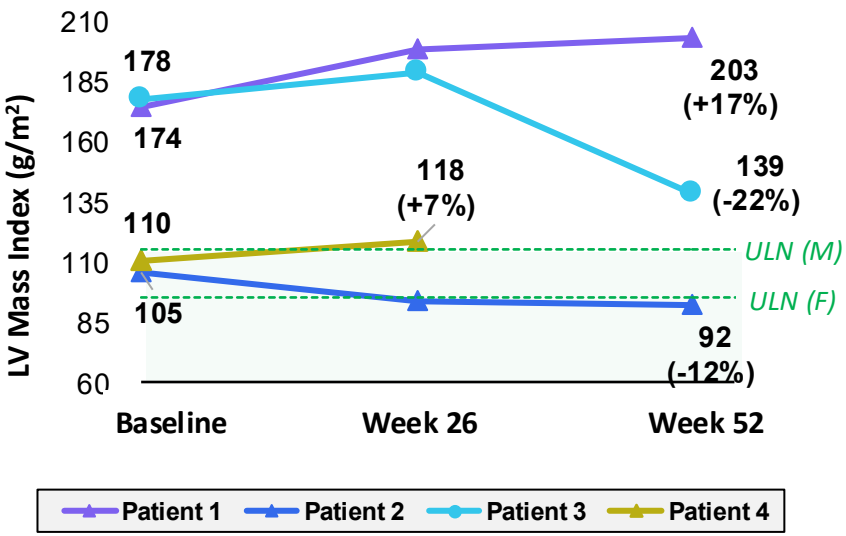
Safety data cut February 2026

Improvements in cardiac structure and HF symptoms observed after 6 months and conclusion of IS

Left Ventricular Posterior Wall Thickness Over Time[1,2]



Left Ventricular Mass Index Over Time[1,2]



- NYHA has improved to Class I in all patients with at least 26 weeks of follow-up

Heart Failure & World Congress on Acute Heart Failure 2026

[1]Desai et al, American Heart Association, 2025
[2]Desai et al. Cardiovascular Research, 2025

HF = heart failure
IS = immunosuppression

Conclusions & future directions for TN-201

WELL TOLERATED

Potential first-in-class gene therapy for HCM remains well tolerated at both 3E13 vg/kg and 6E13 vg/kg doses

OPTIMIZED IMMUNOSUPPRESSION

Changes to the immunosuppression protocol have enabled shorter duration while maintaining stable liver enzyme levels: Oral prednisone dose can be increased and taper restarted from the higher dose, IV pulse steroids (e.g., methylprednisolone for 2-3 days) can be administered, and/or Sirolimus dose and target trough level may be increased (e.g., trough 8 to 12 ng/mL) to facilitate completion of a prolonged corticosteroid taper

INDICATORS OF REMODELING

Directional improvements noted in markers of cardiac structure and heart failure symptoms

MOVE DEVELOPMENT FORWARD

Data support continued dosing of patients and potential expansion into other populations beyond adults, including pediatrics

- MyPEAK-1 patients and their families and co-investigators
- Members of the DSMB: Dr. Barry Greenberg, Dr. Gary Lipshutz, Ena Bromley, and Dr. James Lewis
- Dr. Scott Solomon, Dr. Jon Cunningham and the team at the Cardiovascular Imaging Core Lab at Brigham