HealthCare

GILL HEART & VASCULAR INSTITUTE
Network

CARDIAC AMYLOIDOSIS: RECOGNITION, TREATMENT, AND THE HUMAN STORY

Sonu Abraham, MD, FACC
Assistant Professor, Department of Medicine
Advanced Heart Failure and Transplant Cardiology
Director, Hypertrophic and Infiltrative Cardiomyopathy Program
Gill Heart & Vascular Institute, University of Kentucky

Art Still
Retired NFL Player
Amyloid Patient & Advocate
Still 4 Life

Connecting the Heart of Kentucky

FACULTY DISCLOSURE

- I have no relevant financial relationships with ineligible companies to disclose.

PRESENTATION OBJECTIVES

- After completing this educational activity, participants will be able to:
  - Recognize the clinical features and risk factors associated with cardiac amyloidosis.
  - Review current diagnostic and treatment strategies that can improve outcomes for patients with amyloidosis.
  - Understand the value of patient-centered care through a discussion with former NFL player, Art Still, who will share his personal journey with amyloidosis, from diagnosis through treatment and beyond.

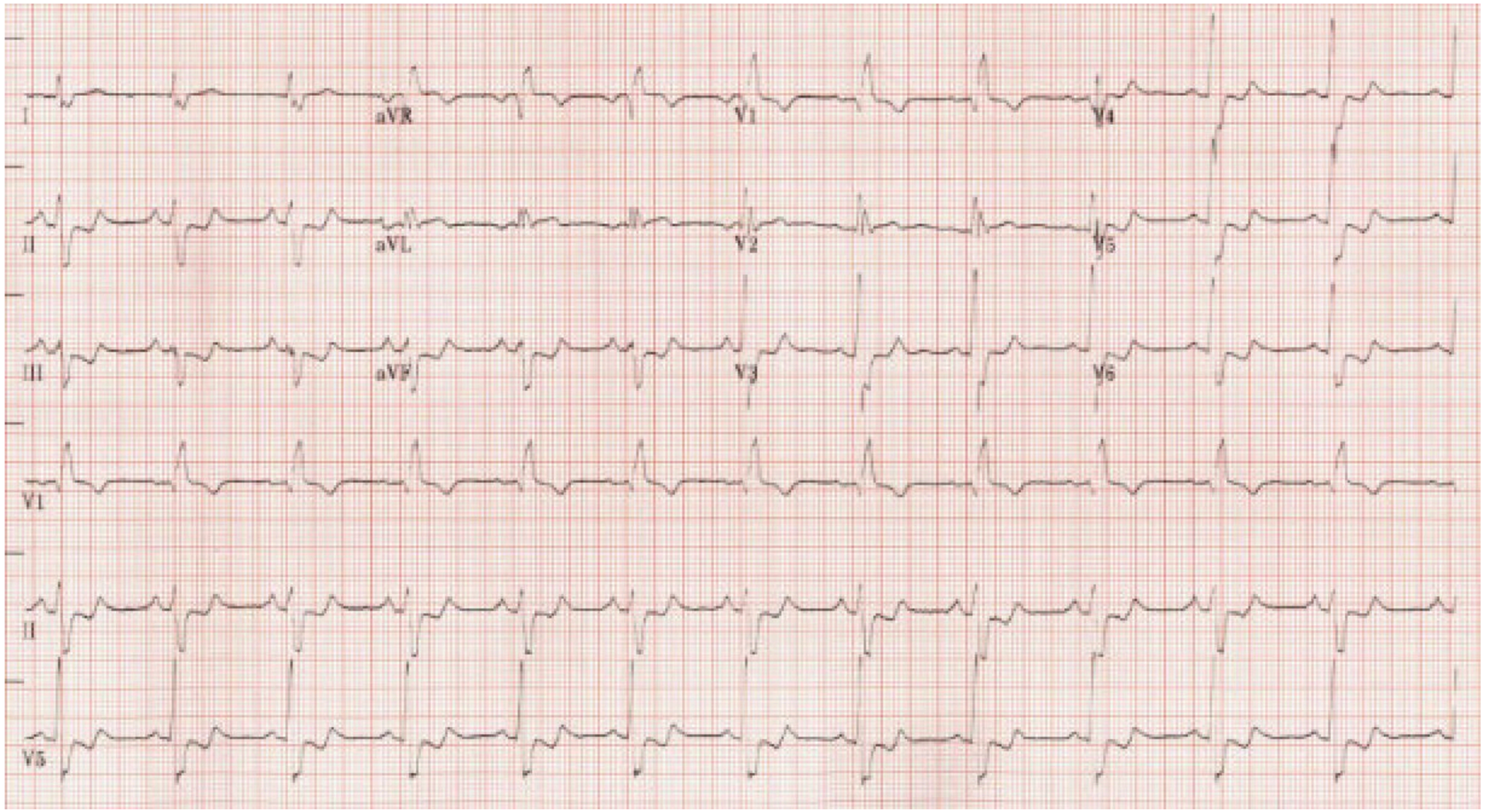
EXPECTED OUTCOME & EDUCATIONAL NEED/ PRACTICE GAP

- **Outcome:** Participants will screen earlier for cardiac amyloidosis in at-risk patients, apply current diagnostic and treatment strategies sooner, and integrate the patient perspective into shared decision-making.
- **Educational Need:** Cardiac amyloidosis is under-recognized and often diagnosed late; many clinicians are not current on evolving diagnostic and treatment options or on the patient experience that shapes outcomes.
- **Practice Gap:** Red flags are missed and workup delayed, versus optimal practice of timely recognition, guideline-based diagnosis and therapy, and patient-centered care informed by the patient journey.

CASE 1

- A 69-year-old male with a past medical history of chronic lymphoid leukemia in remission presented with multiple episodes of pre-syncope referred for concern of hypertrophic cardiomyopathy.
- Other history includes bilateral carpal tunnel syndrome and right biceps tendon rupture.

ELECTROCARDIOGRAM

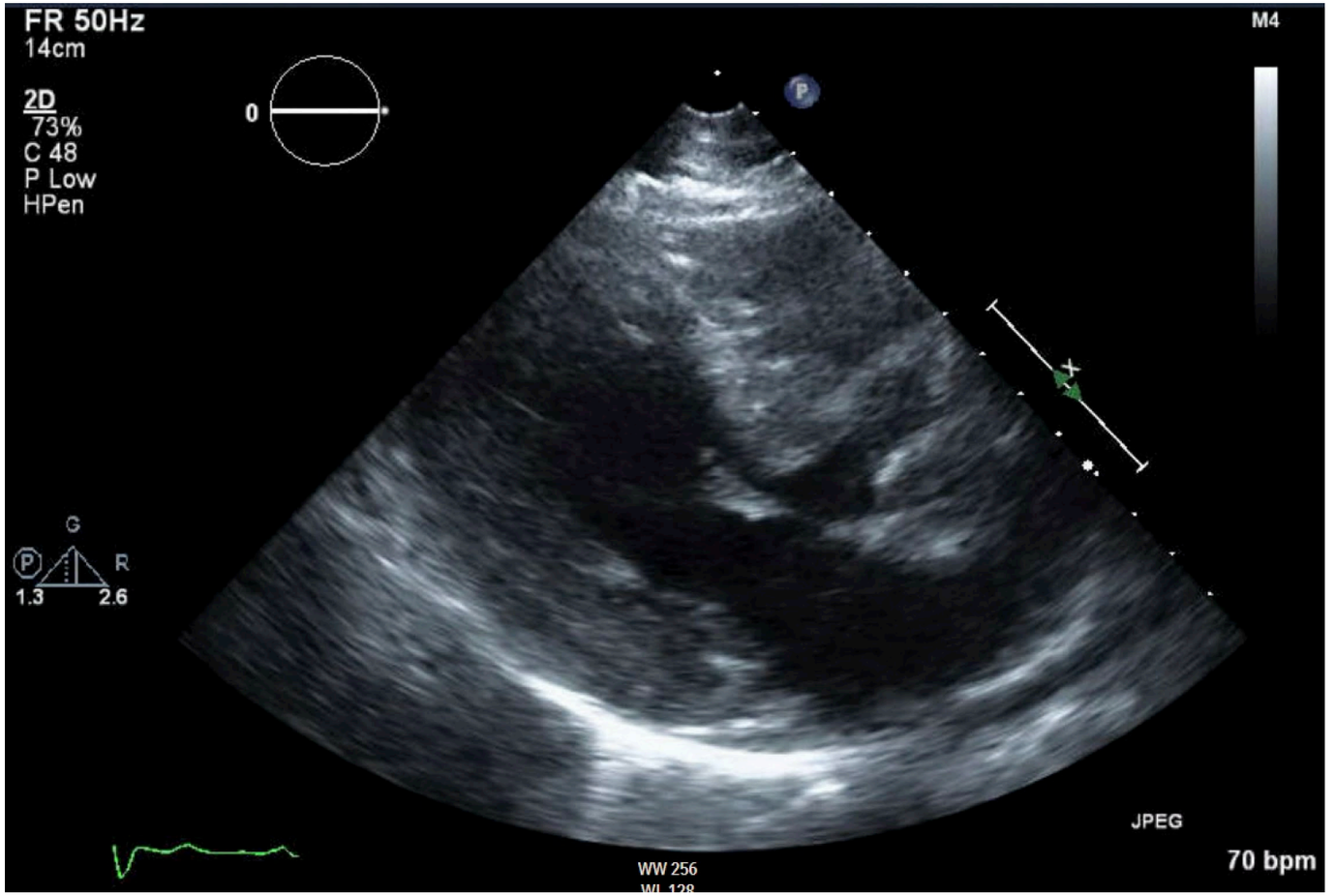


Normal voltage, sinus rhythm and right bundle branch block

UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Connecting the Heart of Kentucky

TRANSTHORACIC ECHOCARDIOGRAM



CASE CONTINUED

- Due to advanced age, concentric left ventricular hypertrophy and history of carpal tunnel syndrome and biceps tendon rupture, an evaluation for cardiac amyloidosis was initiated.

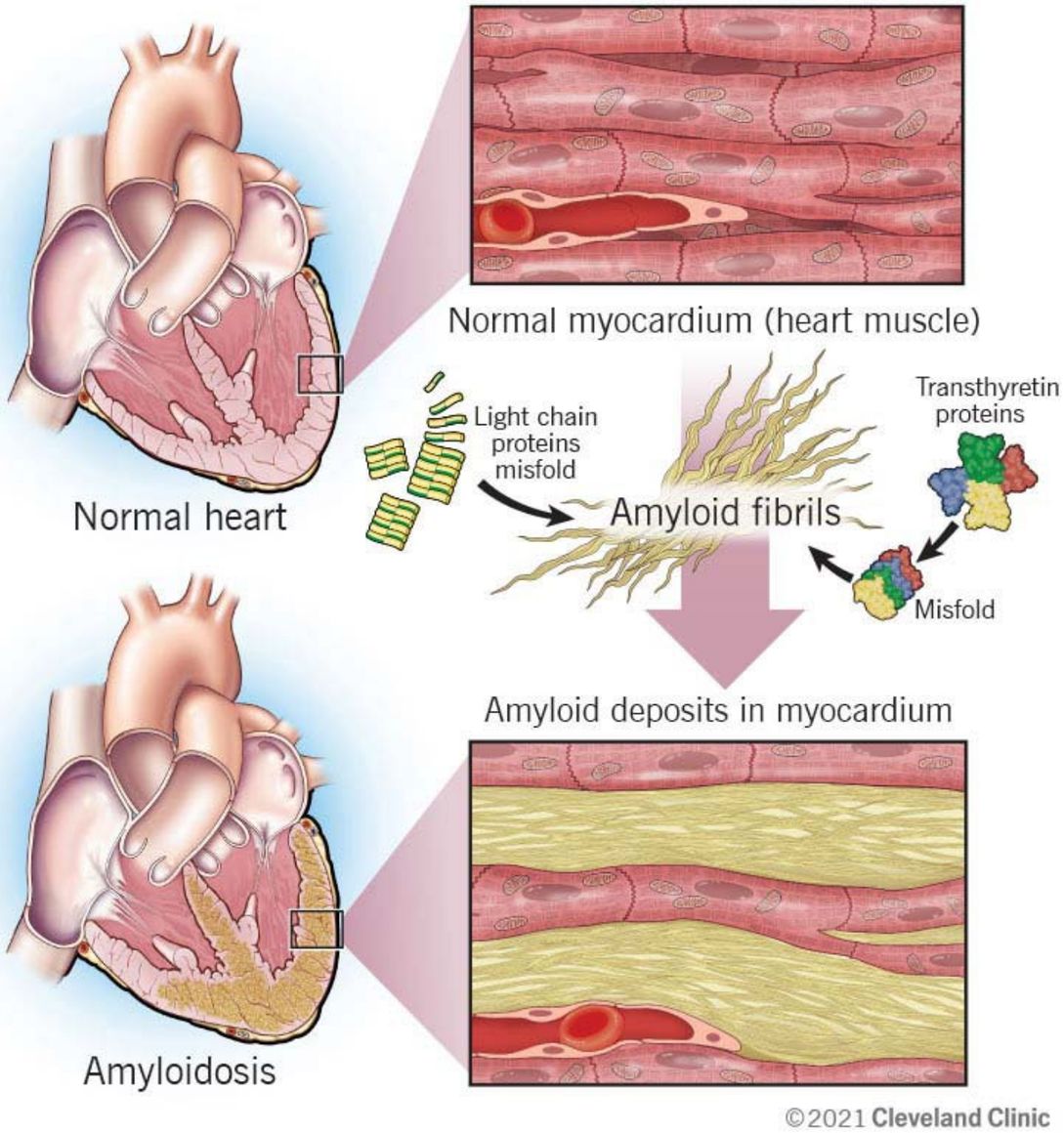
Amyloidosis

UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Connecting the Heart of Kentucky

AMYLOIDOSIS

- Broad spectrum of diseases that result from misfolding of proteins that aggregate into β-sheet amyloid fibrils.
- Over 35 amyloidogenic precursor proteins
- Extracellular deposition of insoluble amyloid fibrils throughout various tissues and organs.
- In cardiac amyloidosis, amyloid fibrils accumulate in the interstitial space between cardiac myocytes, precipitating cellular injury and impairing compliance.

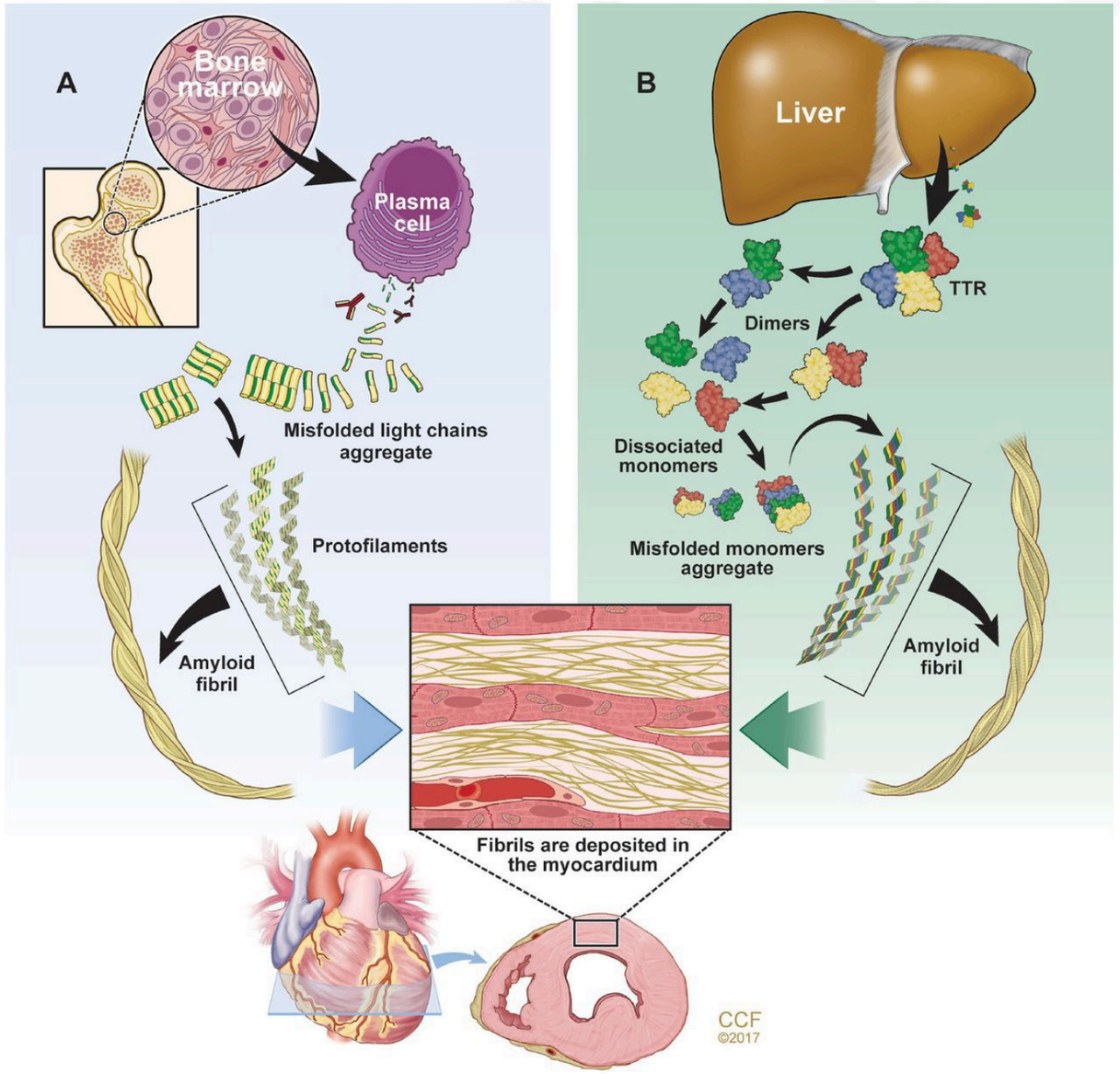


UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Connecting the Heart of Kentucky

Amyloidosis

- Light Chain Amyloidosis
- ATTR amyloidosis
  - Hereditary/variant ATTR amyloidosis
  - Wild-type ATTR amyloidosis



UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Connecting the Heart of Kentucky

ATTR Amyloidosis

UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Connecting the Heart of Kentucky

EPIDEMIOLOGY OF ATTR-CM : TTR CARDIAC AMYLOIDOSIS IS NOT A RARE DISEASE

13% of patients diagnosed with HFpEF and LVH.

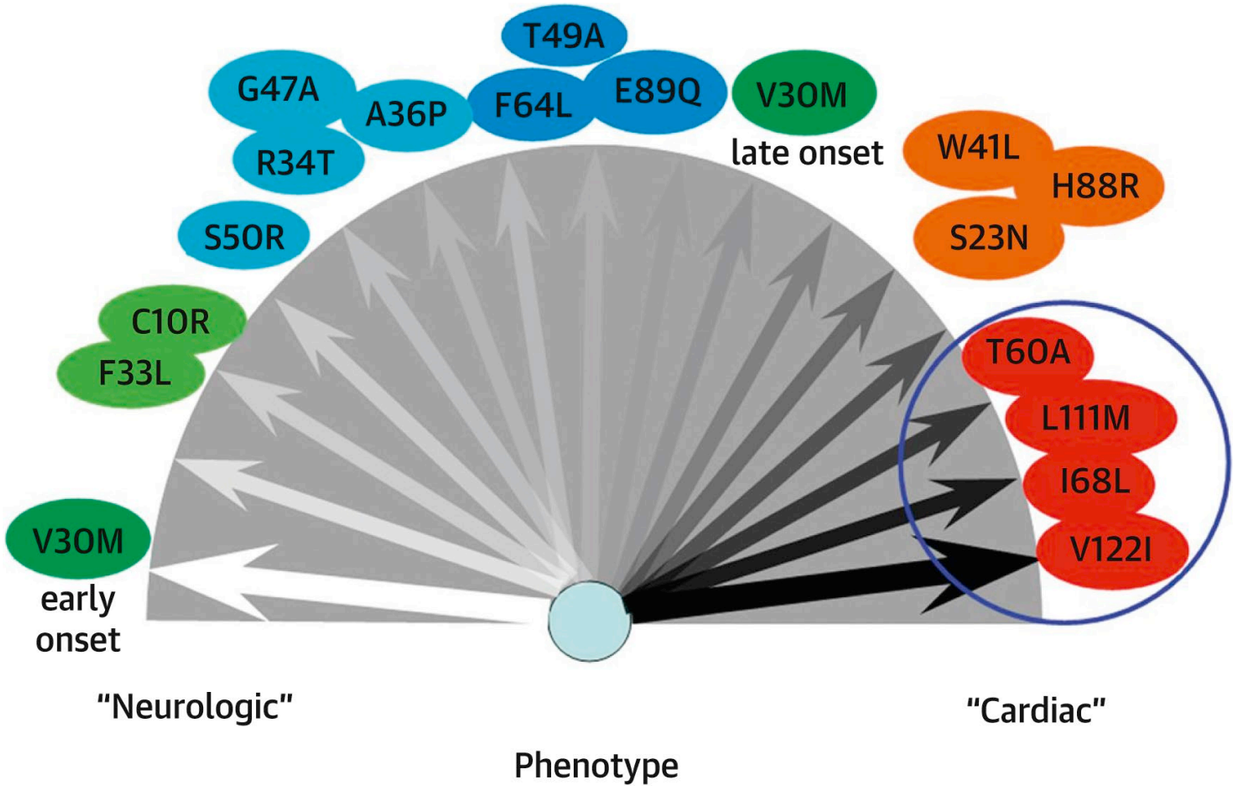
12% of patients with low gradient severe aortic stenosis.

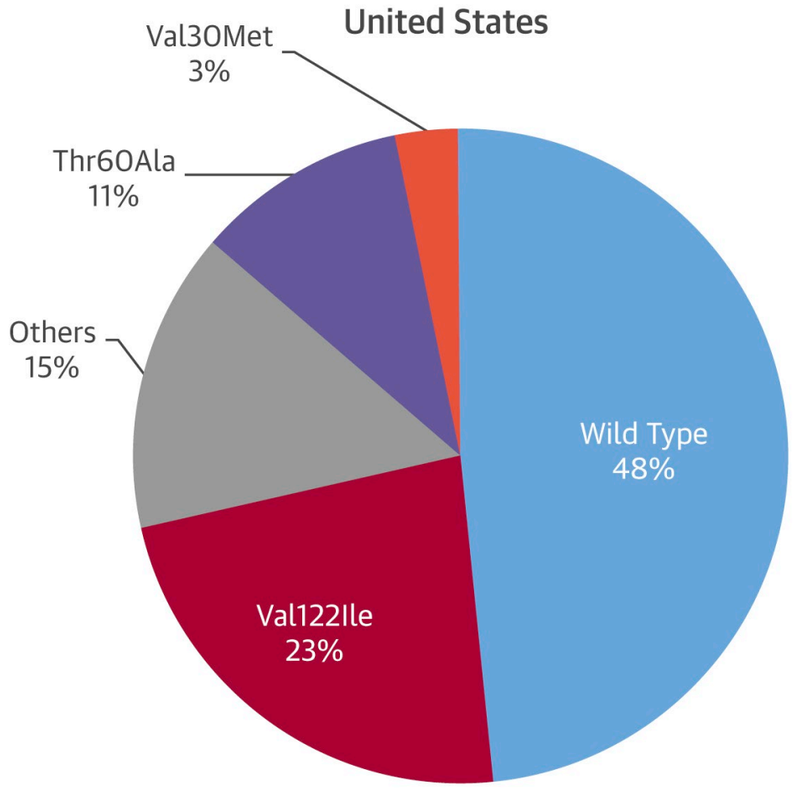
16% of patients with **severe calcific AS undergoing TAVR.**

8.3% of patients (mean age of 77) with a diagnosis of **atrial fibrillation** within a year.

5% of patients with presumed hypertrophic cardiomyopathy

GENOTYPE-PHENOTYPE CORRELATION IN ATTR





HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Maurer MS et al on behalf of the THAOS Investigators. *JACC.* 2016 Jul, 68 (2) 161–172.

Connecting the Heart of Kentucky

GLOBAL DISTRIBUTION OF HEREDITARY ATTR AMYLOIDOSIS

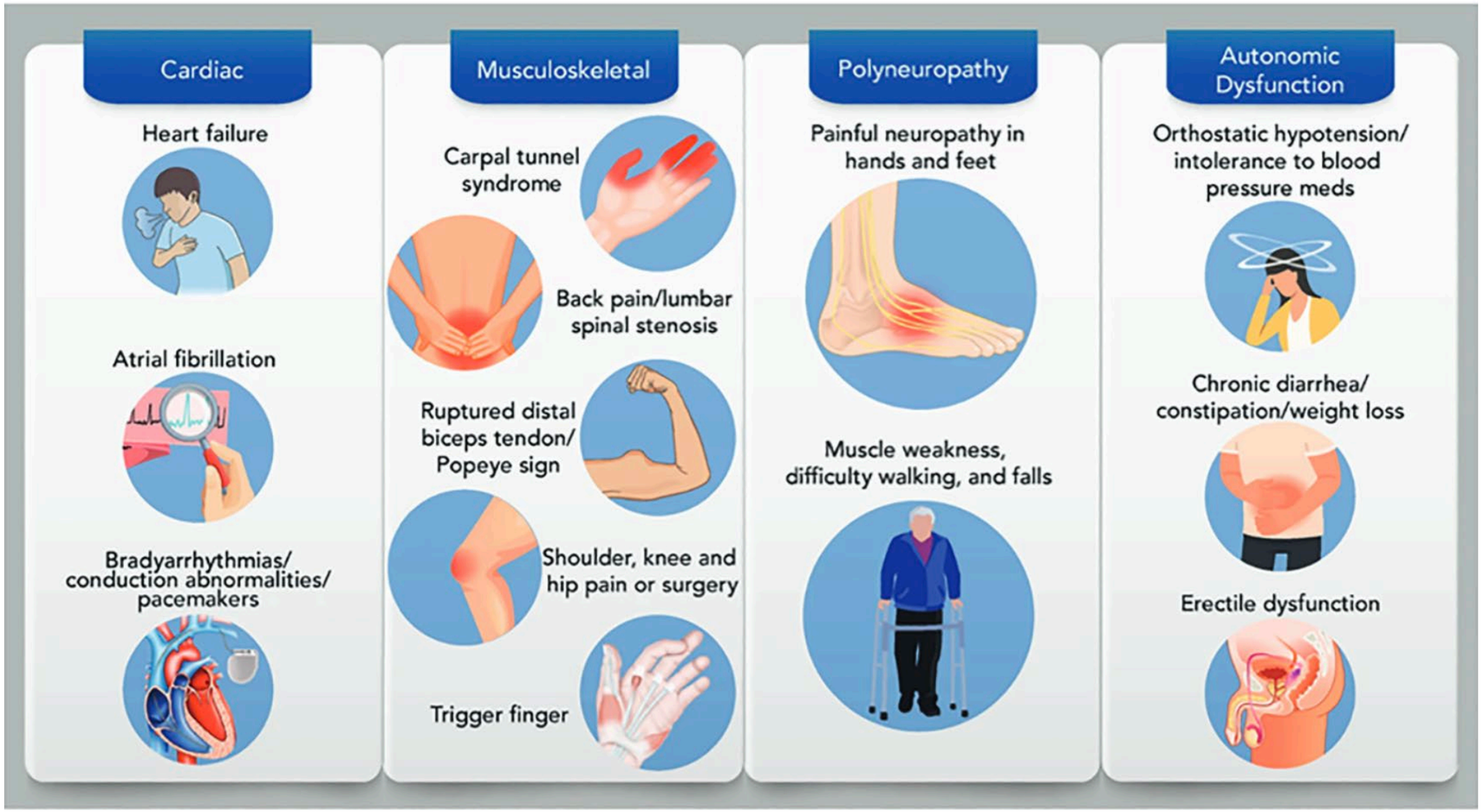


UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Obi CA et al. Methodist Debakey Cardiovasc J. 2022 Mar 14;18(2):17-26.

Connecting the Heart of Kentucky

ATTR AMYLOIDOSIS: CLINICAL MANIFESTATION



UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Writing Committee, Kittleson MM et al. *J Am Coll Cardiol*. 2023;81(11):1076-1126.

Connecting the Heart of Kentucky

REG FLAGS



- Bilateral carpal tunnel syndrome
- Unexplained LVH, low voltage on EKG (discrepant EKG)
- New diagnosis of HCM >60 years of age
- Orthostatic hypotension and unexplained neuropathic pain
- Recurrent atrial fibrillation in an older adult that is difficult to treat
- Persistently elevated troponins, with CAD ruled out multiple times
- Hypertension that is ”cured” as the patient gets older leading to discontinuation of anti-hypertensives.

WATCH OUT FOR THE CLUES

TABLE 1 Clues Suggesting a Diagnosis of Cardiac Amyloidosis

Cardiac Manifestations	Extracardiac Manifestations
Clinical	**Musculoskeletal**
■ Fatigue	■ Bilateral carpal tunnel syndrome
■ Heart failure symptoms	■ Lumbar/cervical spinal stenosis
■ Family history of heart failure	■ Spontaneous biceps tendon rupture
Electrical	■ Hip or knee replacement
■ Conduction system disease/pacemaker	**Neurologic**
■ Atrial fibrillation	■ Peripheral neuropathy
■ Pseudoinfarct pattern	■ Family history of neuropathy
■ Discordant QRS voltage for degree of increased left ventricular wall thickness on imaging	■ Autonomic dysfunction
Imaging	■ Intolerance to vasodilating antihypertensive medications
■ Increased left ventricular wall thickness	■ Orthostatic hypotension
■ Grade 2 or worse diastolic function	■ Gastroparesis
■ Abnormal longitudinal strain with apical sparing	■ Urinary incontinence
■ Diffuse subendocardial or transmural late gadolinium enhancement on cardiac magnetic resonance imaging with increased extracellular volume fraction	■ Erectile dysfunction
Laboratories	**Renal**
■ Persistent low-level troponin elevation	■ Nephrotic syndrome
■ Elevated B-type natriuretic peptide or N-terminal pro–B-type natriuretic peptide	

Writing Committee, Kittleson MM et al. *J Am Coll Cardiol*. 2023;81(11):1076-1126.

CARPAL TUNNEL SYNDROME

- **10%** of men age >50 years and women >60 years undergoing carpal tunnel release surgery for idiopathic CTS had amyloidosis diagnosed from tenosynovial tissue biopsy.

- Screening for CA in patients with prior surgery for bilateral CTS finds **approximately 5%** with early-stage transthyretin CA. The clinical yield was higher **(>1 in 5)** when focusing on **nonobese men ≥70 years**, showing potential for systematic screening.

Sperry BW et al. *J Am Coll Cardiol*. 2018;72(17):2040-2050. Westin O et al. *J Am Coll Cardiol*. 2022;80(10):967-977.

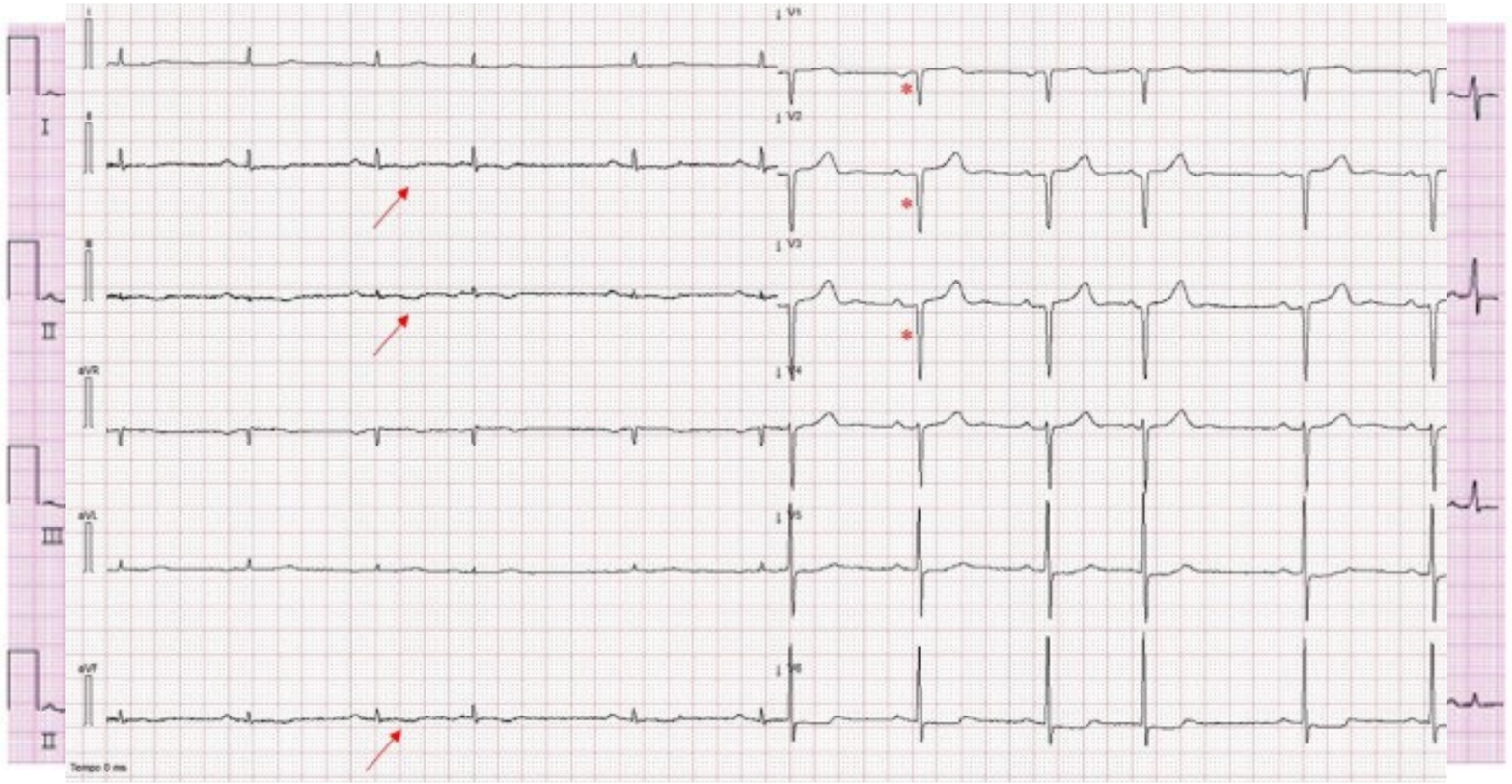
DELAYS IN DIAGNOSIS OF CARDIAC AMYLOIDOSIS

- Many patients see **more than 5 physicians** before receiving a correct diagnosis!!!
- In a survey of patients with ATTR-CM, diagnosis was made **within 6 months** of symptom onset in **only 35%** of those with ATTRv and **46%** of those with ATTRwt.
- Requires high degree of suspicion

Lousada I et al. Orphanet J Rare Dis. 2015 Nov 2;10(Suppl 1):P22.

ELECTROCARDIOGRAM

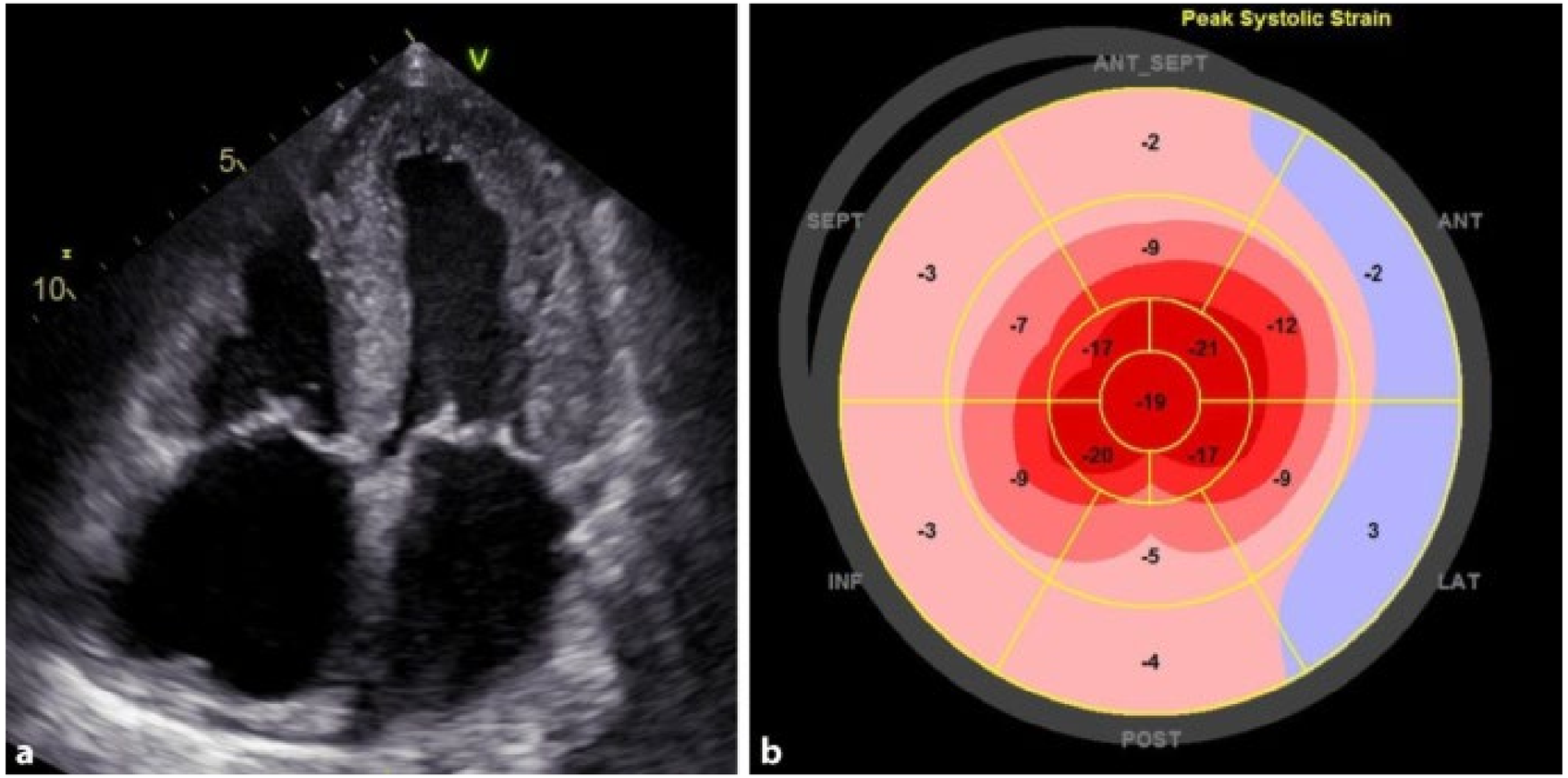
- Low voltage ECG – **NOT AS COMMON** in cardiac amyloidosis!!!
- AL amyloidosis – 55%
- ATTR amyloidosis – 35%
- Pseudoinfarct pattern - more common – 70%
- Sinus node dysfunction & AV blocks : most frequent causes of pacemaker implantation in patients with CA.



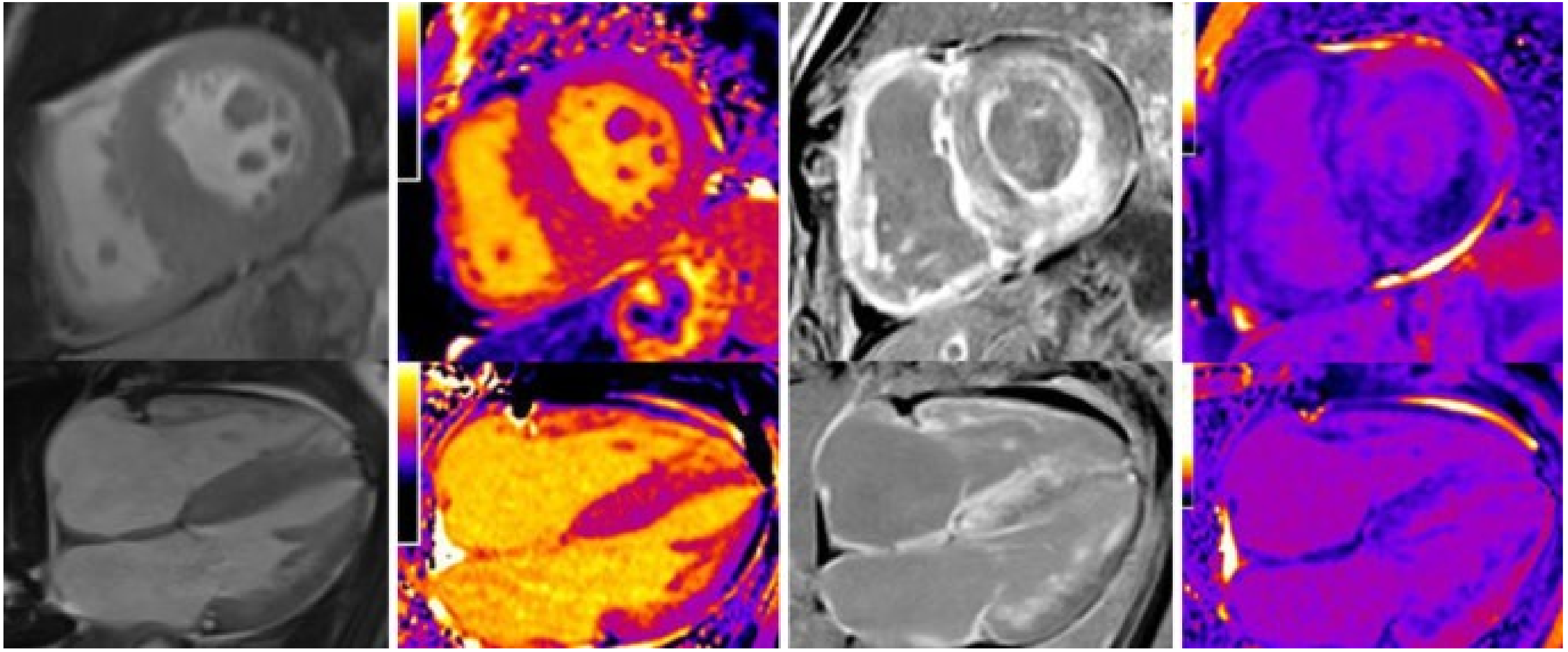
UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Connecting the Heart of Kentucky

ECHOCARDIOGRAM



CARDIAC MRI



HealthCare

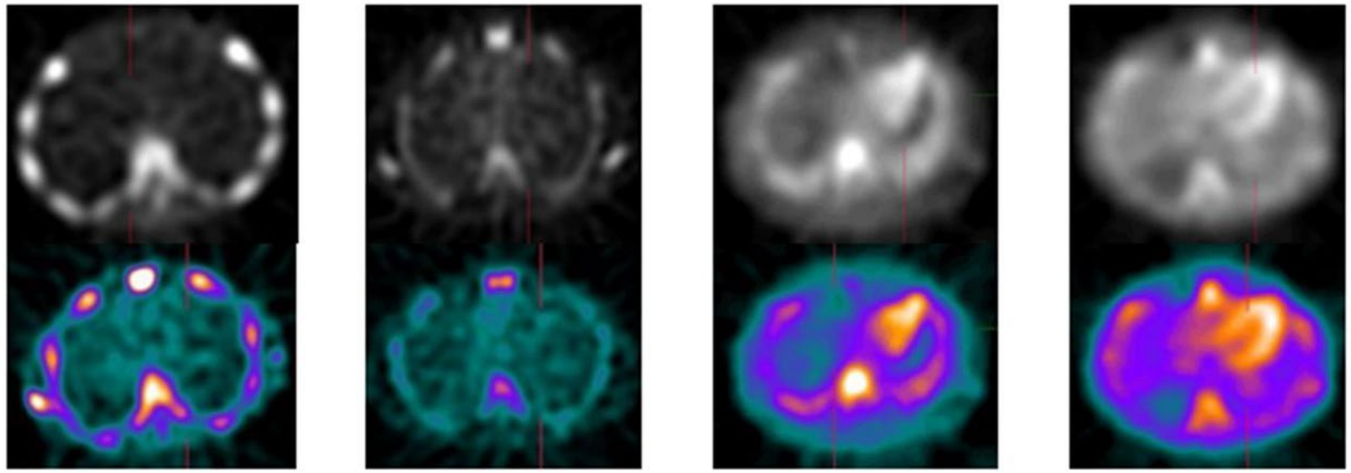
GILL HEART & VASCULAR INSTITUTE

Network

Connecting the Heart of Kentucky

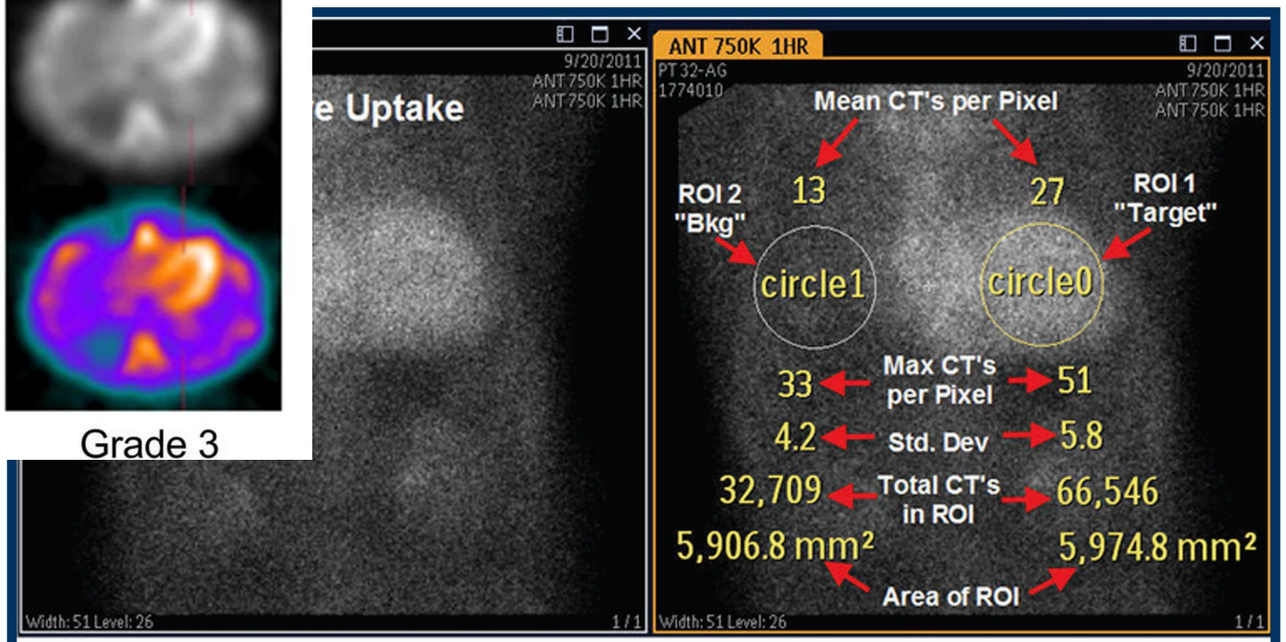
NUCLEAR TECHNETIUM PYROPHOSPHATE SCAN

SPECT ^{99m}Tc-PYP visual scoring:



Grade 0 Grade 1 Grade 2 Grade 3

Grade 0	No uptake and normal bone uptake
Grade 1	Uptake less than rib uptake
Grade 2	Uptake equal to rib uptake
Grade 3	Uptake greater than rib uptake with mild/absent rib uptake

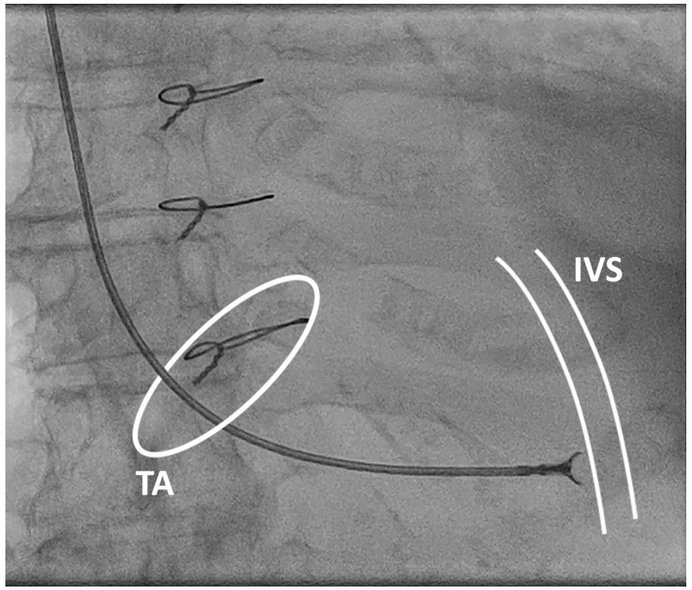


Biopsy proven ATTR cardiac amyloidosis with H/CL = 2.08

HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

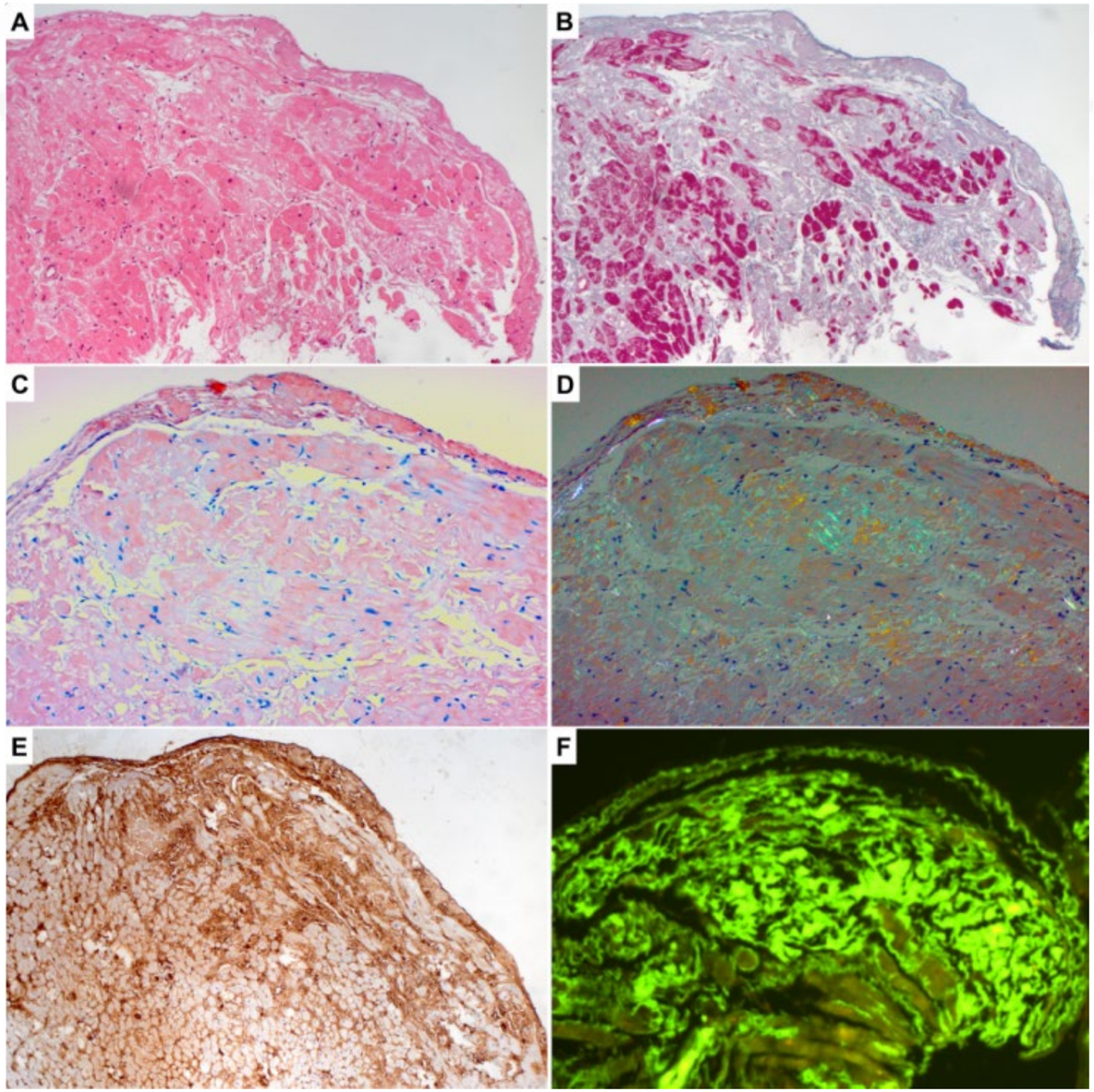
Connecting the Heart of Kentucky

ENDOMYOCARDIAL BIOPSY



Apple Green Birefringence –

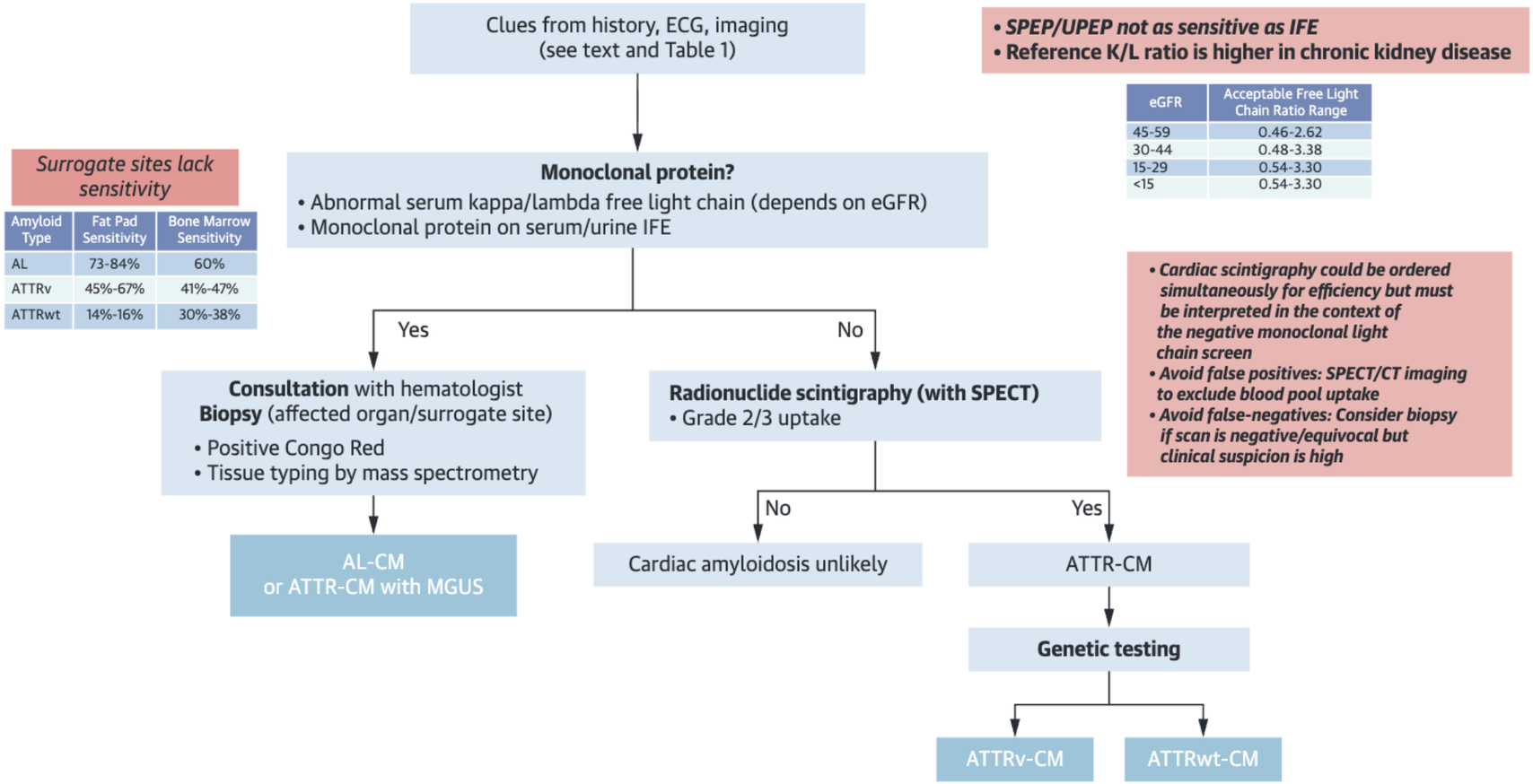
Congo red staining



UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Connecting the Heart of Kentucky

DIAGNOSTIC ALGORITHM FOR CARDIAC AMYLOIDOSIS



eGFR	Acceptable Free Light Chain Ratio Range
45-59	0.46-2.62
30-44	0.48-3.38
15-29	0.54-3.30
<15	0.54-3.30

Amyloid Type	Fat Pad Sensitivity	Bone Marrow Sensitivity
AL	73-84%	60%
ATTRv	45%-67%	41%-47%
ATTRwt	14%-16%	30%-38%

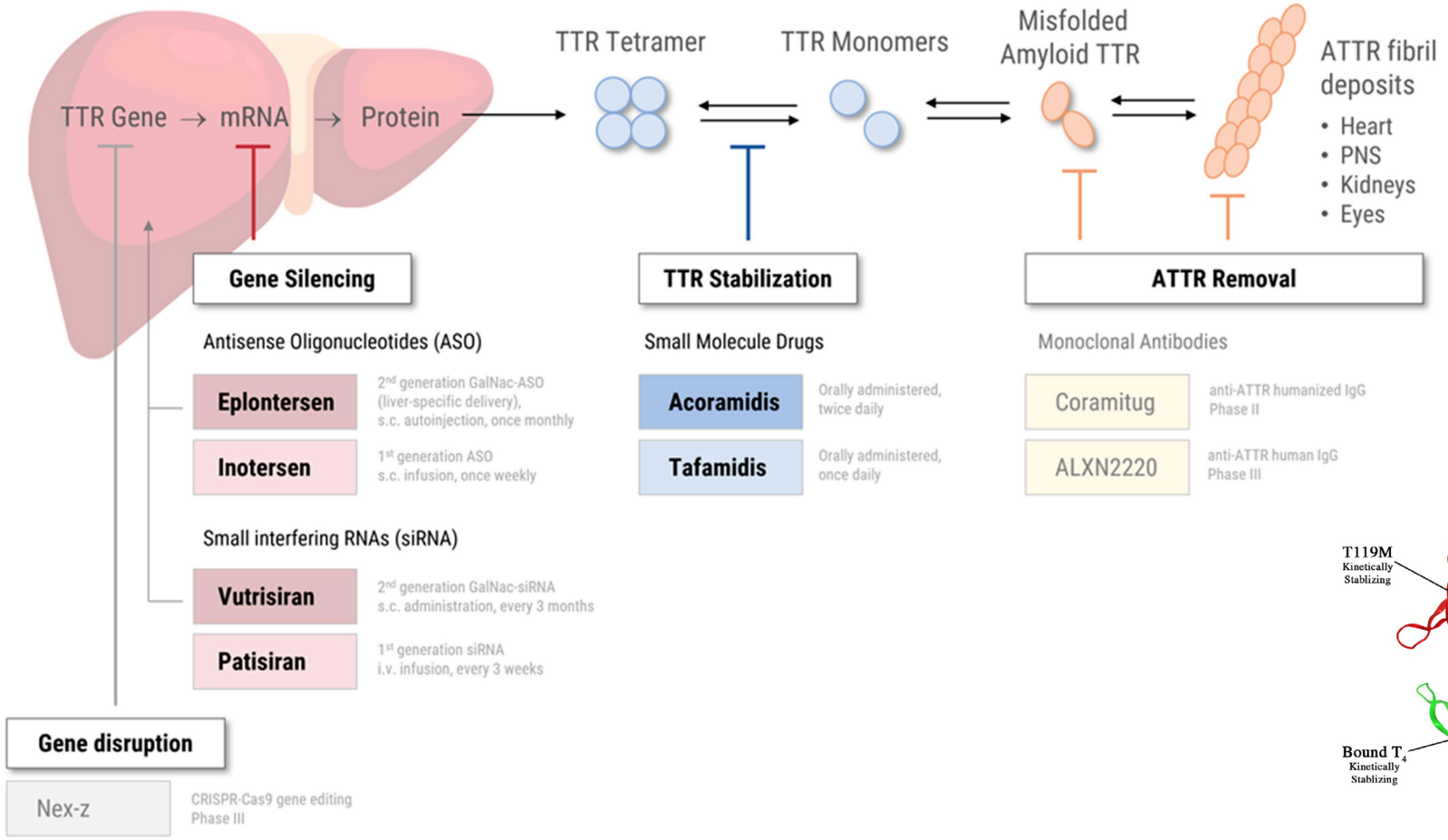
Writing Committee, Kittleson MM et al. *J Am Coll Cardiol*. 2026 Feb, 87 (5) 549–565.

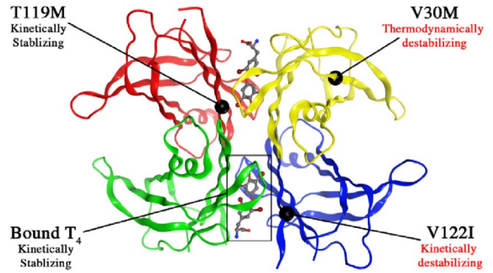
PROGNOSTICATION OF ATTR CARDIAC AMYLOIDOSIS

National Amyloidosis Center staging		Mayo staging	
NAC I 69.2 months	NT-proBNP ≤3,000 ng/L and eGFR ≥45 ml/min	Mayo I 57 months	NT-proBNP ≤3,000 ng/L and hs-cTnT ≤65 ng/L
NAC II 46.7 months	Either NT-proBNP >3,000 ng/L or eGFR <45 ml/min	Mayo II 42 months	Either NT-proBNP >3,000 ng/L or hs-cTnT >65 ng/L
NAC III 24.1 months	NT-proBNP >3,000 ng/L and eGFR<45ml/min	Mayo III 18 months	NT-proBNP>3,000ng/L and hs-cTnT >65 ng/L

Müller ML et al. *JACC Adv*. 2025;4(2):101568.

TREATMENT OPTIONS FOR ATTR AMYLOIDOSIS





UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

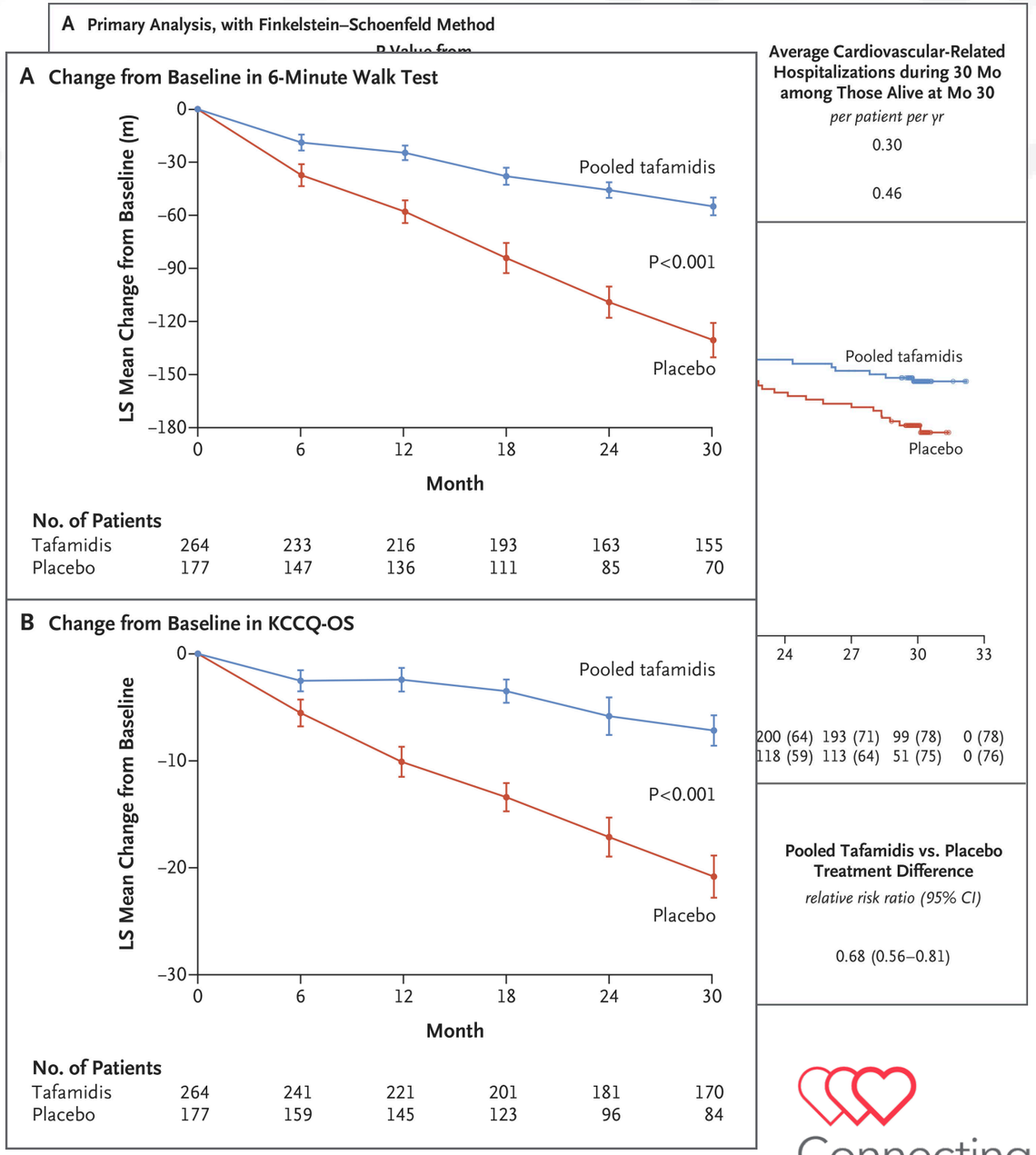
Tschöpe, C et al. *J. Clin. Med.* **2025**, *14*, 4785.

Connecting the Heart of Kentucky

ATTR-ACT TRIAL

TAFAMIDIS: small-molecule drug that specifically binds to the T4-binding site of TTR

- 441 patients
- 2:1:2 ratio to receive 80 mg of tafamidis, 20 mg of tafamidis, or placebo for 30 months.
- Hierarchically assessed all-cause mortality, followed by frequency of cardiovascular-related hospitalizations.
- The median age 75 years
- Predominantly male
- 24% ATTRv (Val122Ile, Thr60Ala, and Ile68Leu most common mutations)
- 33% mortality reduction (p=0.018)
- NNT: 7-8 per one death over 2 ½ years



UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Connecting the Heart of Kentucky

ATTRIBUTE-CM TRIAL

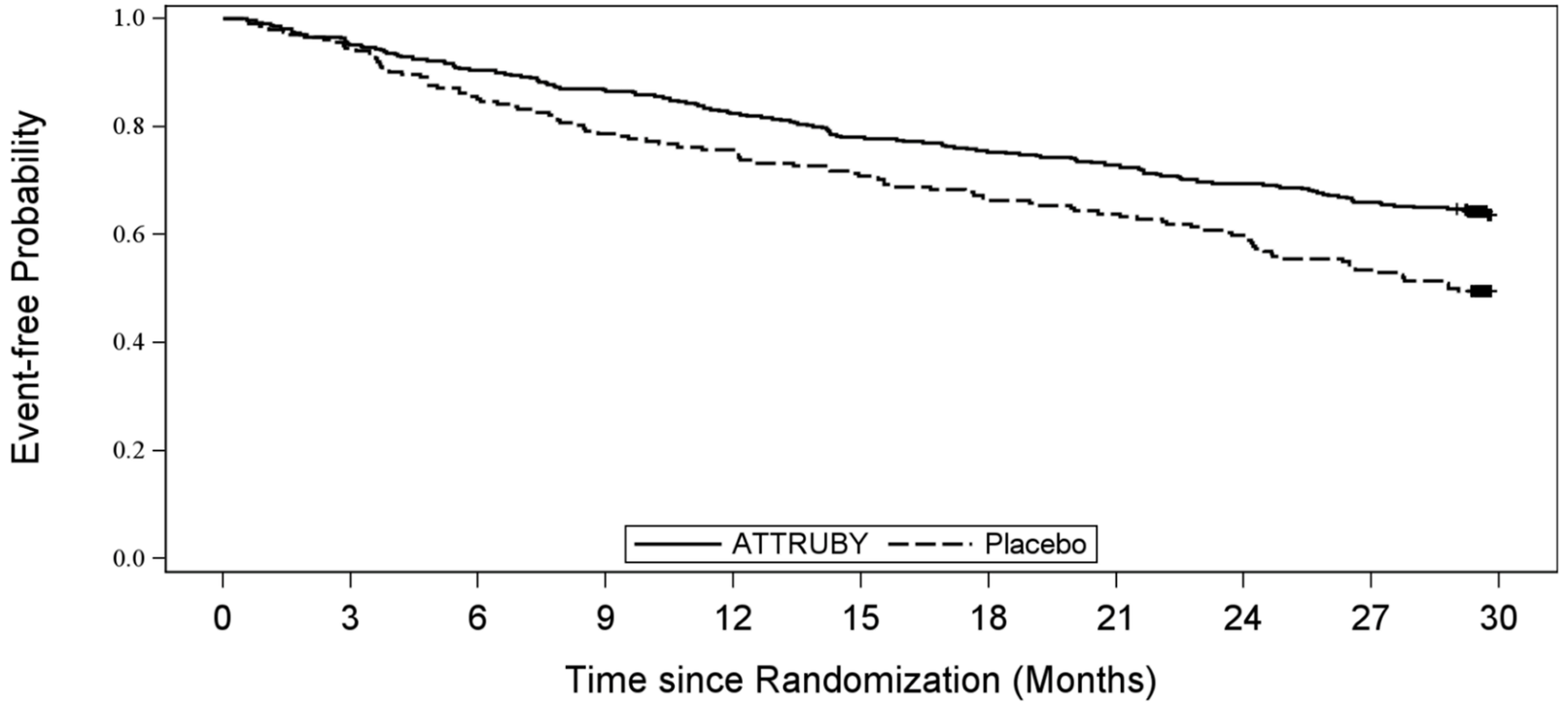
ACORAMID
intermo

iant. By reinforcing
thermodynamic

Hierarchi

	P Value
Death fror hospital	2.2) <0.001
Death fror hospital	1.8)
Death fror hospital	2.0)

Figure 3: Time to First All-cause Mortality or Cardiovascular-Related Hospitalization over Month 30, mITT Population



Subjects Remaining at Risk (Cumulative Events)

ATTRUBY	409 (0)	389 (20)	370 (39)	355 (54)	337 (72)	319 (90)	308 (101)	298 (111)	284 (125)	270 (139)	0 (147)
Placebo	202 (0)	191 (11)	172 (30)	159 (43)	152 (50)	143 (59)	135 (67)	129 (73)	121 (81)	108 (94)	0 (102)

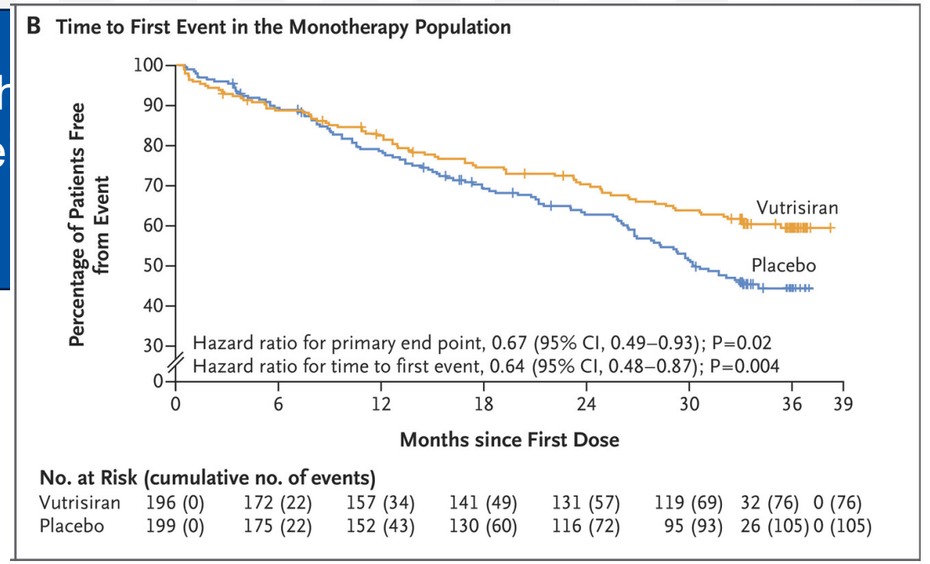
HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

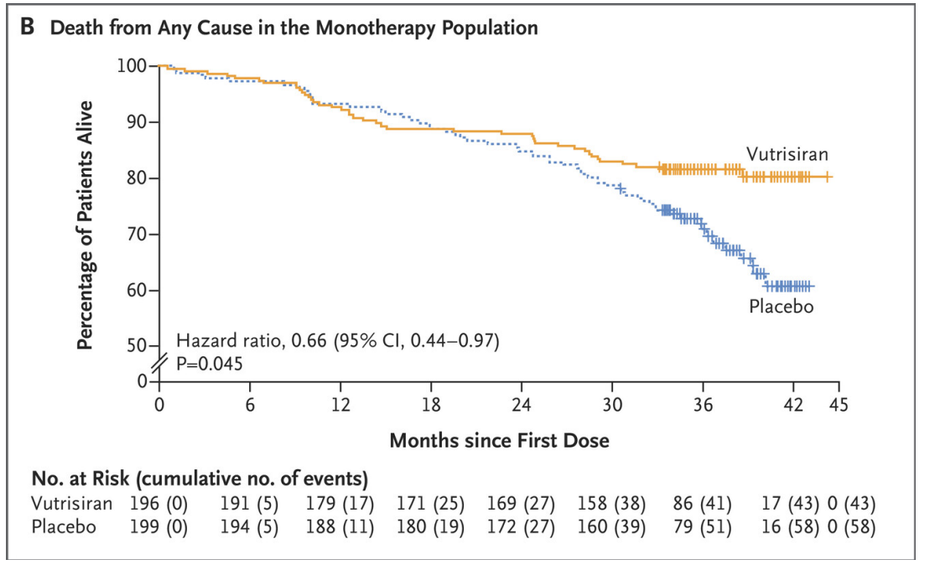
Connecting the Heart of Kentucky

HELIOS-B TRIAL

VUTRISIRAN: Subcutaneously administered RNA interference th
synthesis of both wild-type and variant *TTR* messenger RNA at the
of the pathogenic protein before amyloid-causing

- 655 patients
- 1:1 ratio to receive vutrisiran (25 mg) or placebo every 12 weeks for up to 36 months.
- Primary end point : composite of death from any cause and recurrent cardiovascular events (defined as hospitalizations for cardiovascular causes or urgent visits for heart failure)

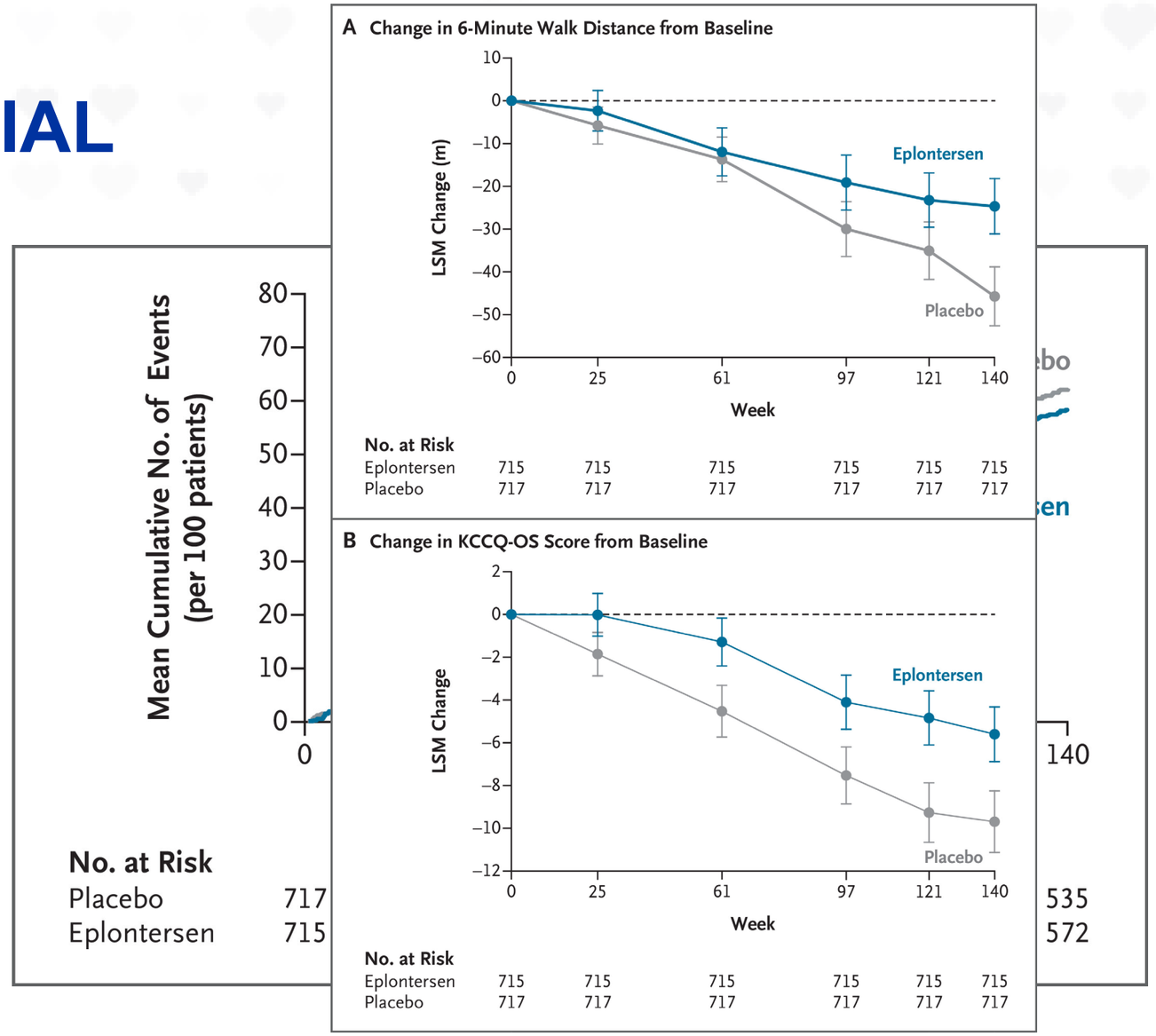




HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

CARDIO-TTRANSFORM TRIAL

- 1432 patients
- 1:1 ratio, patients with ATTR-CM to receive subcutaneous eplontersen (45 mg) or placebo every 4 weeks for 140 weeks, in addition to standard treatment.
- Primary end point: cumulative composite of death from cardiovascular causes and recurrent cardiovascular clinical events up to week 140.
- 57% of patients were on TTR stabilizer therapy at baseline

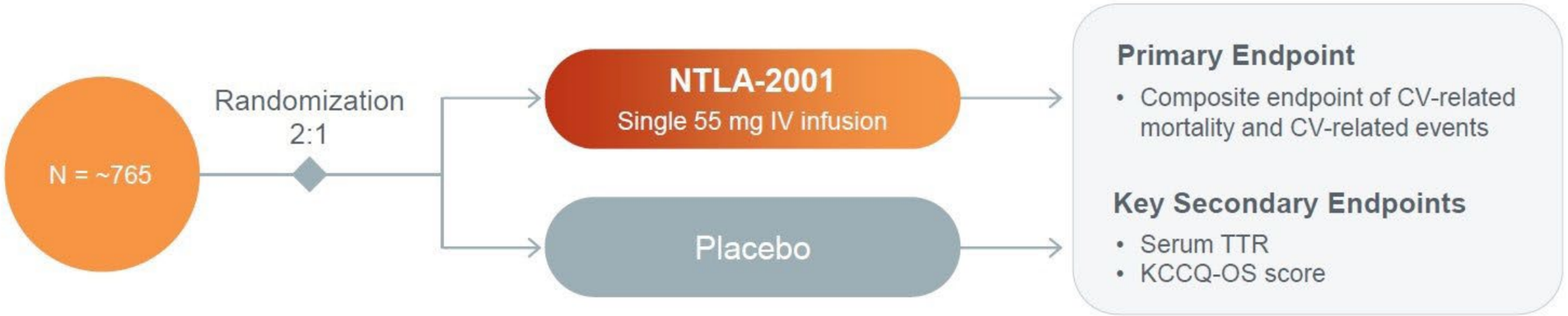


HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Connecting the Heart of Kentucky

MAGNITUDE
ATTR-CM

A Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate NTLA-2001 in Patients with ATTR Amyloidosis with Cardiomyopathy (ATTR-CM)



Key Eligibility Criteria:

- Adult patients with diagnosis of either hereditary or wild-type ATTR-CM
- NYHA Class I – III
- NT-proBNP baseline ≥ 1000 pg/mL

Stratification:

- NAC stage
- TTR genotype: wild-type vs. mutant
- Concomitant tafamidis use vs. no tafamidis

Study Duration:

- Dependent on occurrence of pre-specified number of CV events and a minimum of 18 months follow-up
- Majority of patients are expected to have ≥ 30 months of follow-up for the primary analysis

Clinicaltrials.gov ID: NCT06128629

REGENERON Intellia THERAPEUTICS

UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

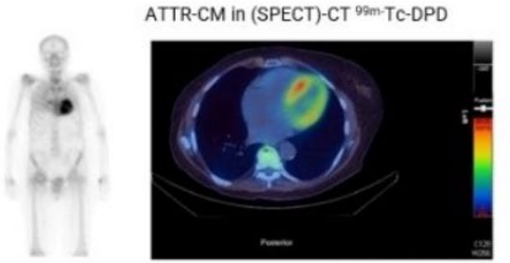
Connecting the Heart of Kentucky

TTR DEPLETE – PHASE 1B STUDY

ALXN2220 (cliramitug) for the depletion of cardiac transthyretin amyloid (ATTR)

ATTR cardiomyopathy

- Infiltrative, progressively invalidating and fatal disease
- Extracellular deposition of ATTR increases cardiac wall thickness and stiffness, impairing systolic and diastolic function
- No treatment available to directly reduce cardiac amyloid load



ATTR-CM in (SPECT)-CT ^{99m}-Tc-DPD

Sabharwal *Heart* 2017

Cliramitug (formerly ALXN2220, NI006)

- Investigational human anti-ATTR antibody
- Designed to deplete ATTR amyloid from tissue
- Selective for misfolded transthyretin [1]
- IV infusion, administered every 4 weeks (q4w)
- NI006-101: Phase 1b study in patients with ATTR-CM [2]

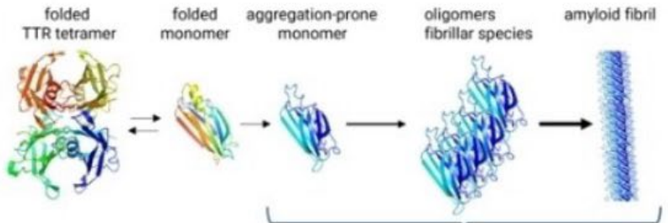


Figure adopted from Azevedo *Amyloidosis* 2013

[1] Michalon *Nature Communications* 2021, [2] Garcia-Pavia *NEJM* 2023

Efficacy and safety of cliramitug currently being investigated in the Phase 3 Study: DepleTTR-CM

GENERAL HF MANAGEMENT

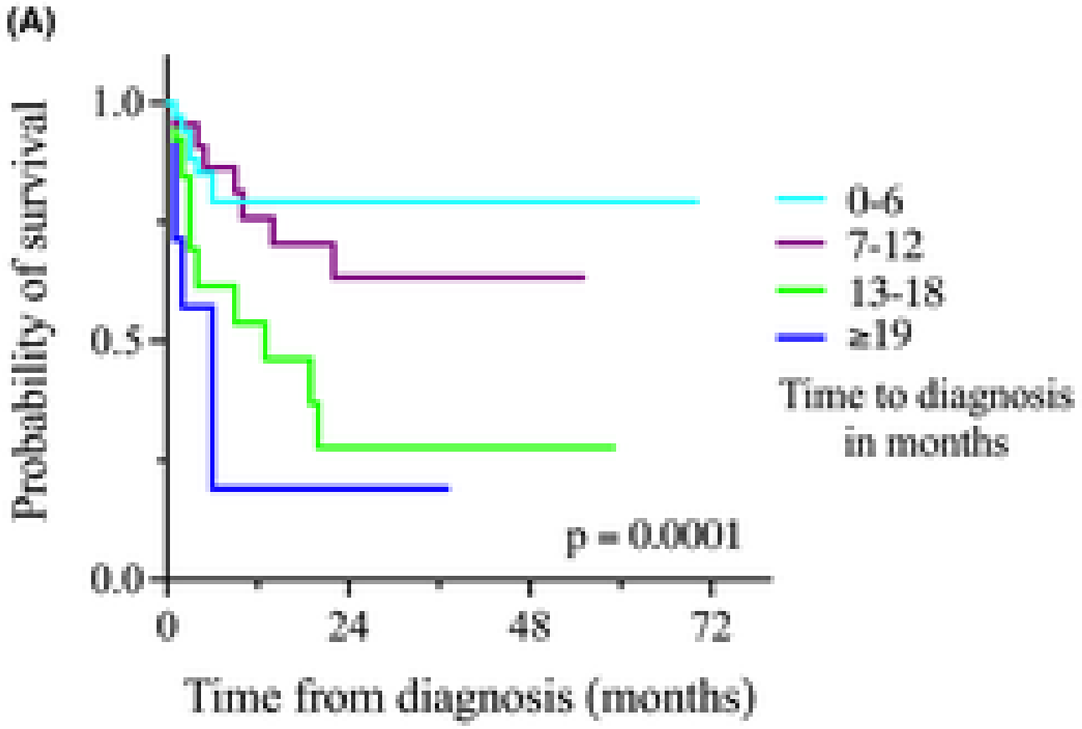
- Stop digoxin and non-dihydropyridine calcium channel blockers*
- Beta blockers may be avoided*
- ACEI/ARBs may not be tolerated due to associated orthostatic hypotension
- Diuretics + spironolactone: Mainstay
- Observational data supports use of SGLT2 inhibitors
- Anticoagulation for atrial fibrillation regardless of CHADSVASc score

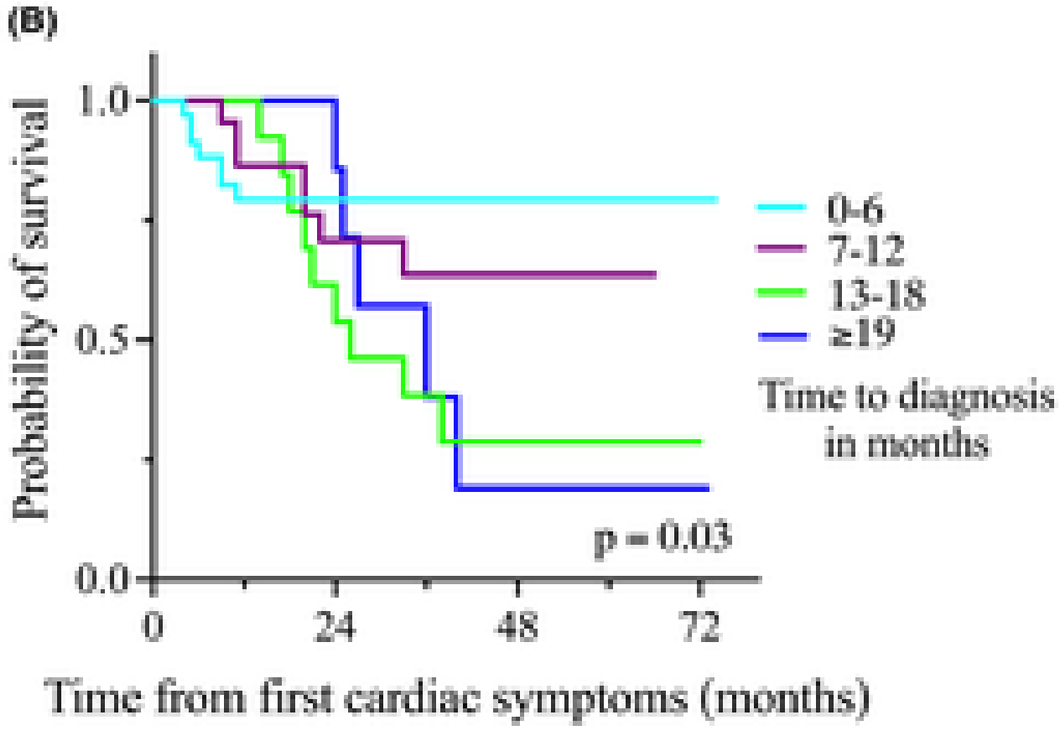
AL Amyloidosis

UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Connecting the Heart of Kentucky

AL AMYLOIDOSIS: URGENT MANAGEMENT!!!



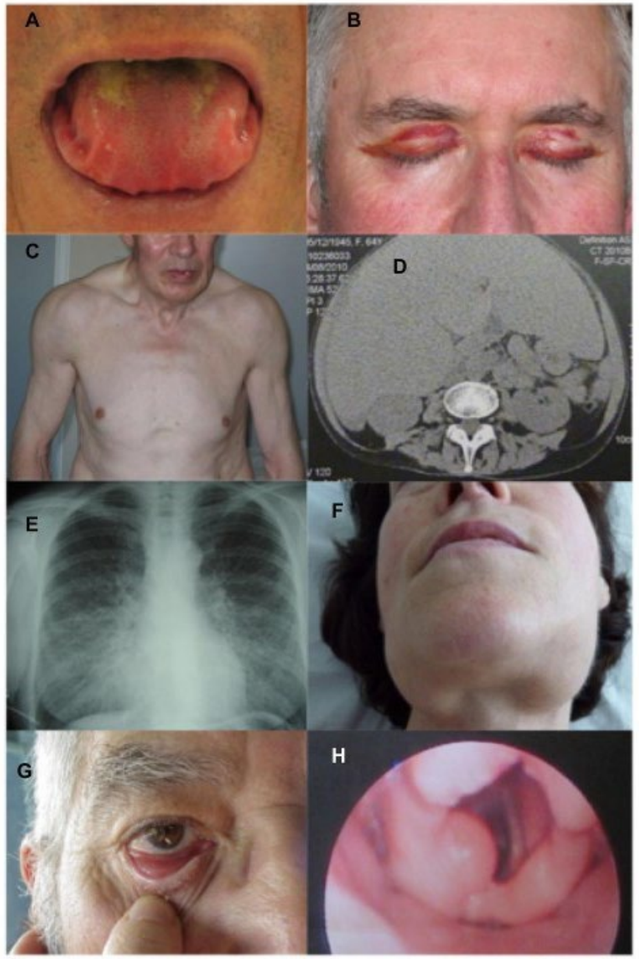


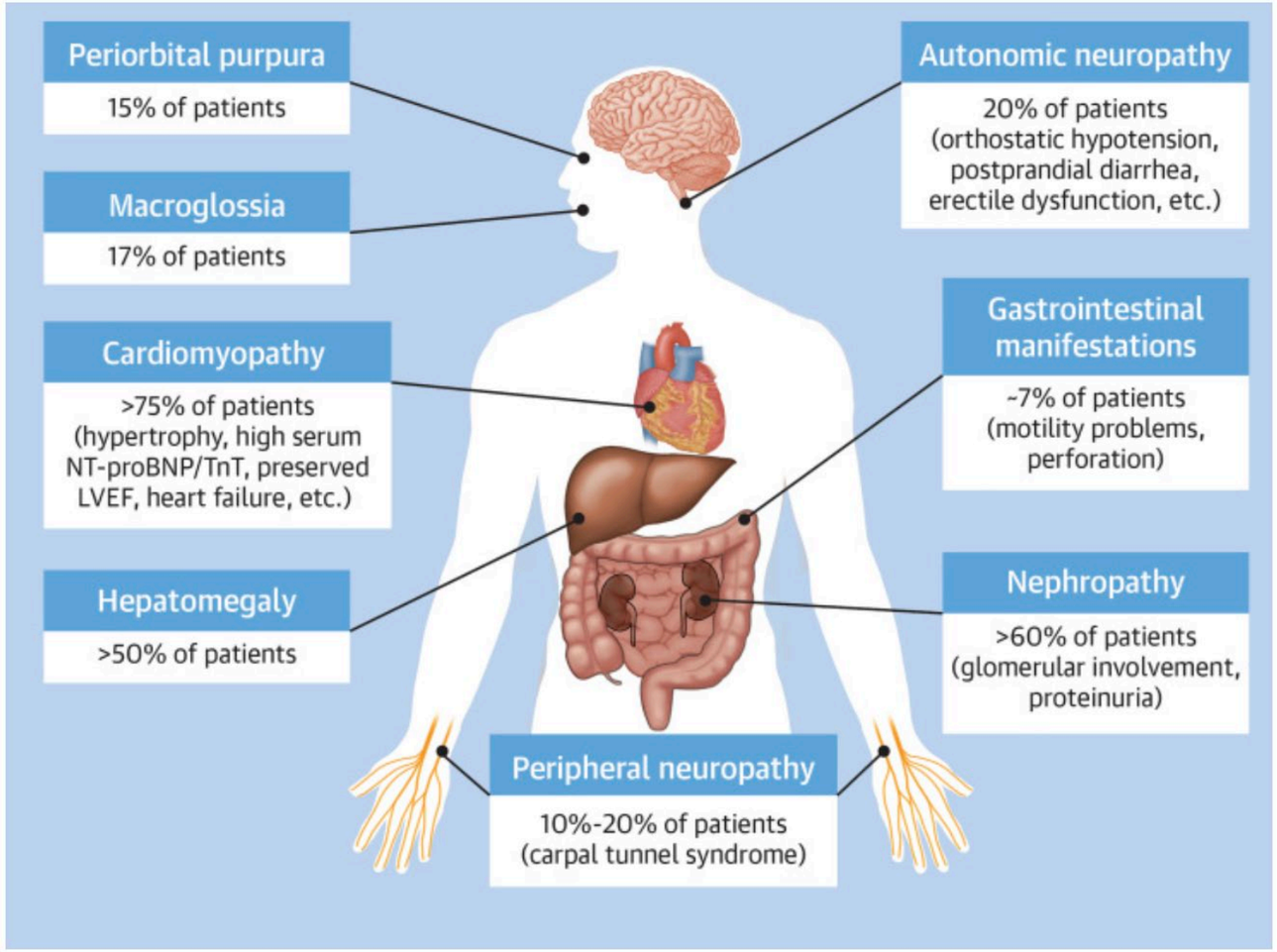
UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Oubari S et al. *Eur J Haematol*. 2021;107(4):449-457.

Connecting the Heart of Kentucky

SYSTEMIC MANIFESTATIONS OF AL AMYLOIDOSIS



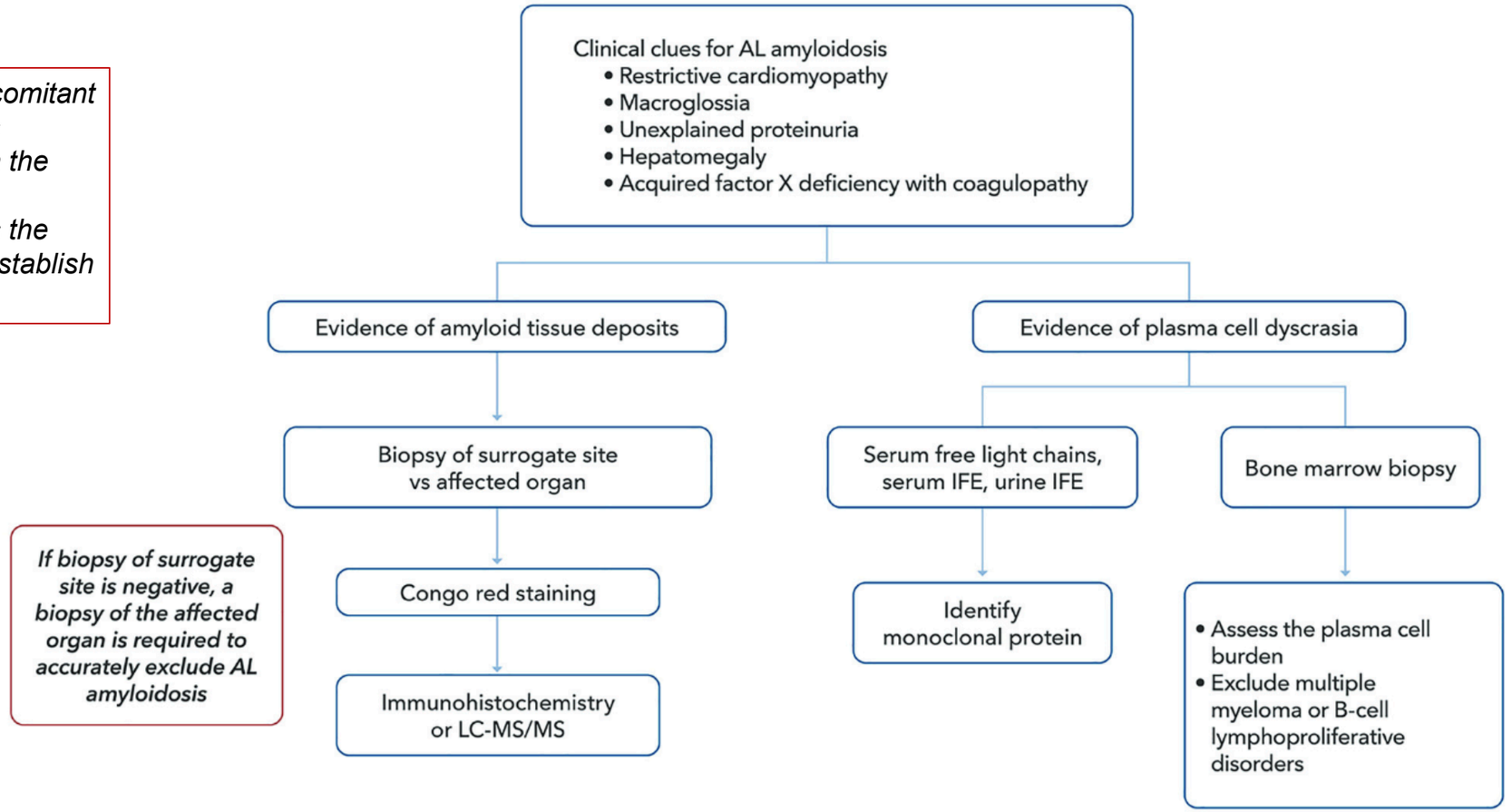


UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Connecting the Heart of Kentucky

DIAGNOSIS OF AL AMYLOIDOSIS

In situations of suspected concomitant systemic AL and ATTR cardiac amyloidosis (such as MGUS in the context of abnormal nuclear scintigraphy), cardiac biopsy is the preferred route to definitively establish the cardiac pathology.



UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Writing Committee, Kittleson MM et al. *J Am Coll Cardiol*. 2023;81(11):1076-1126.

Connecting the Heart of Kentucky

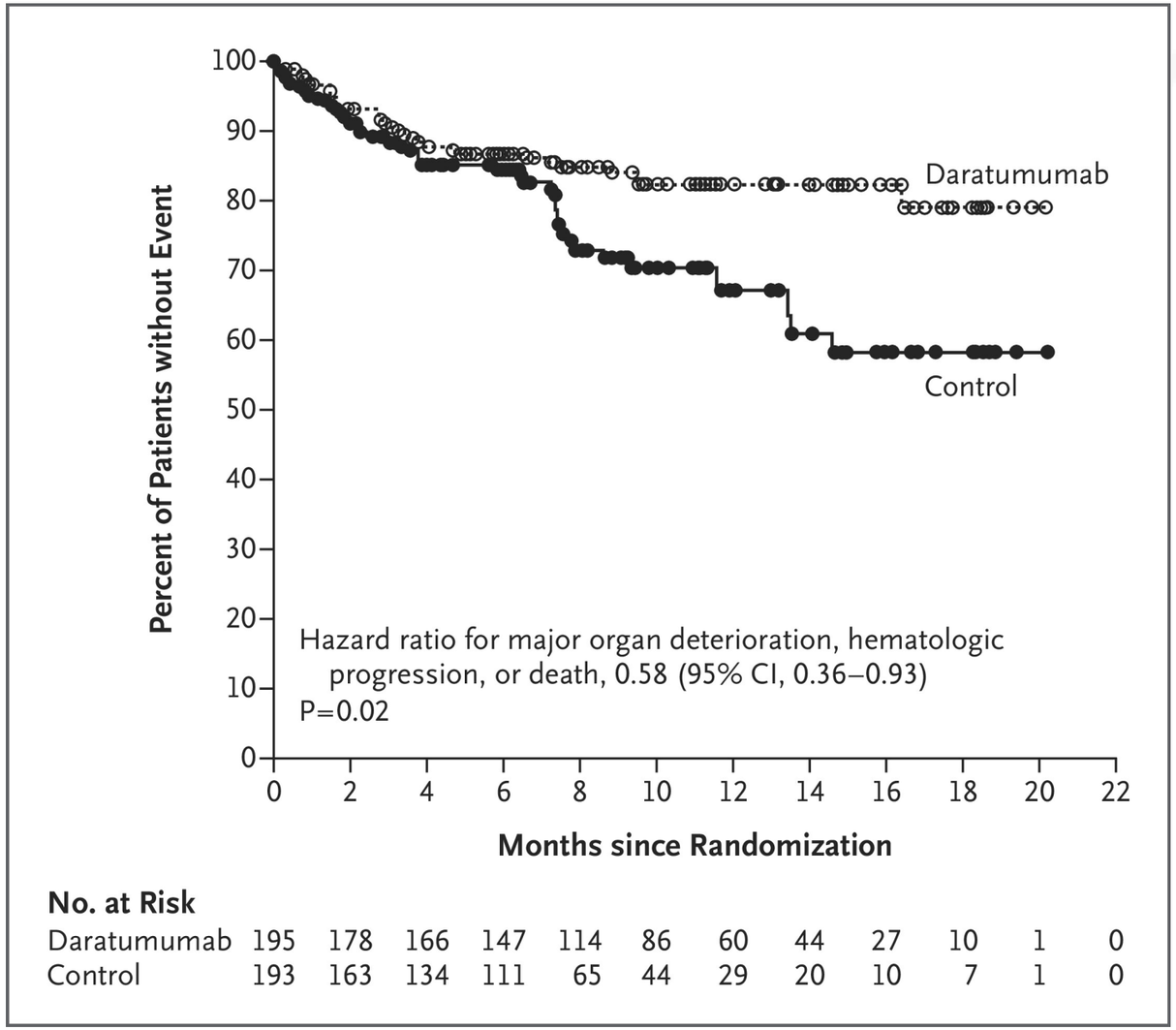
STAGING OF AL AMYLOIDOSIS

Mayo Clinic (2004) Integrating European Collaborative Study 3B Staging					Mayo Clinic (2012)				
Risk factors	Risk factors present (n)	Stage	Patients (%)	Median OS (mos)	Risk factors	Risk factors present (n)	Stage	Patients (%)	Median OS (mos)
cTnT >0.035 ng/mL NT-proBNP >332 pg/mL	0	1	33	86	cTnT >0.025 ng/mL NT-proBNP >1,800 pg/mL dFLC >180 mg/L	0	1	25	94.1
	1	2	30	43		1	2	27	40.4
	2	3A	18	17		2	3	25	14
	NT-proBNP ≥8,500 pg/mL	3B	19	4.6		3	4	23	5.8

ANDROMEDA TRIAL

DARATUMUMAB: a human CD38-targeting antibody

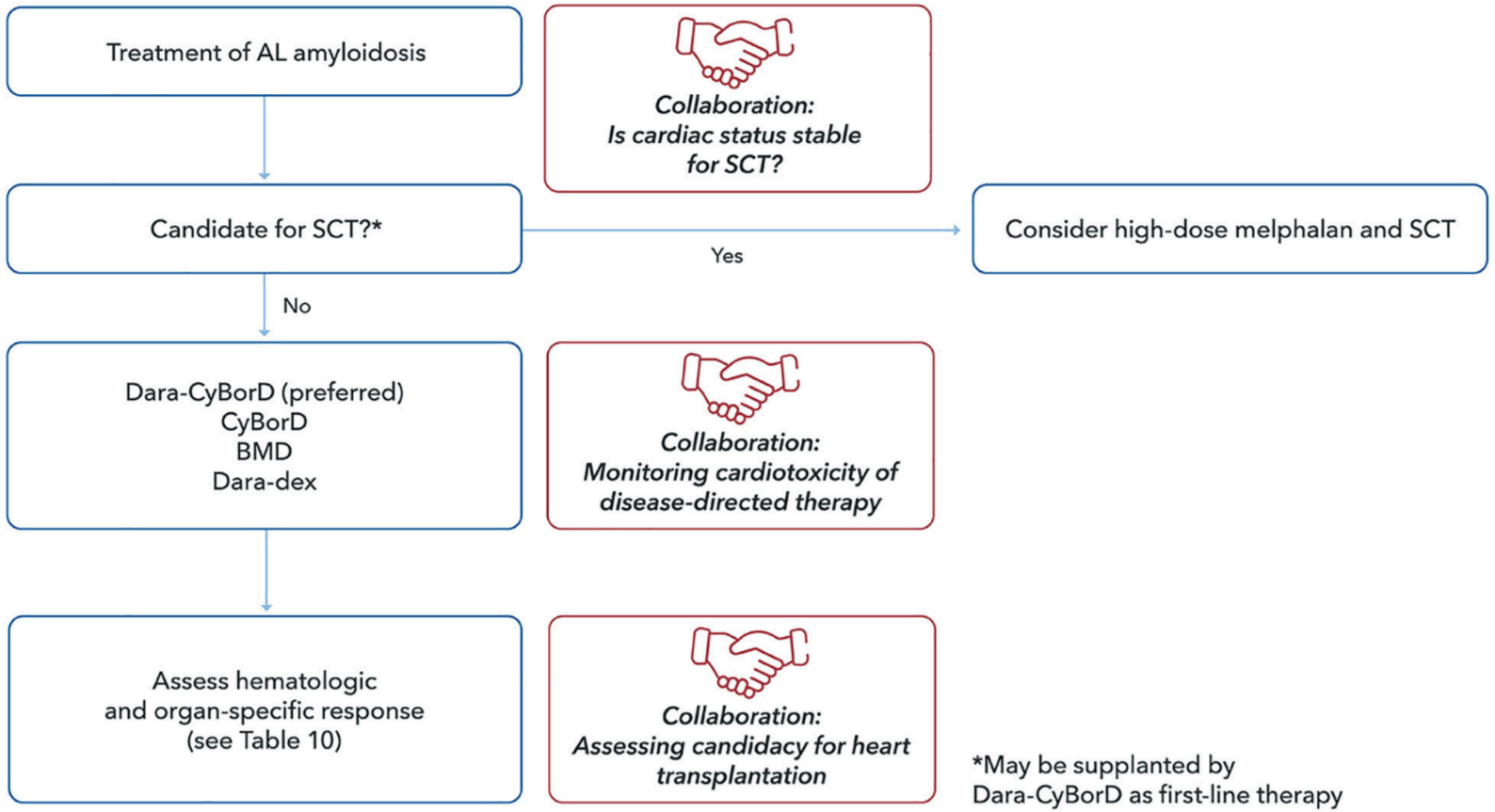
- 388 patients
- Patients with newly diagnosed AL amyloidosis to receive six cycles of bortezomib, cyclophosphamide, and dexamethasone either alone (control group) or with subcutaneous daratumumab followed by single-agent daratumumab every 4 weeks for up to 24 cycles (daratumumab group)



UK HealthCare
GILL HEART & VASCULAR INSTITUTE
Network

Connecting the Heart of Kentucky

TREATMENT OF AL AMYLOIDOSIS

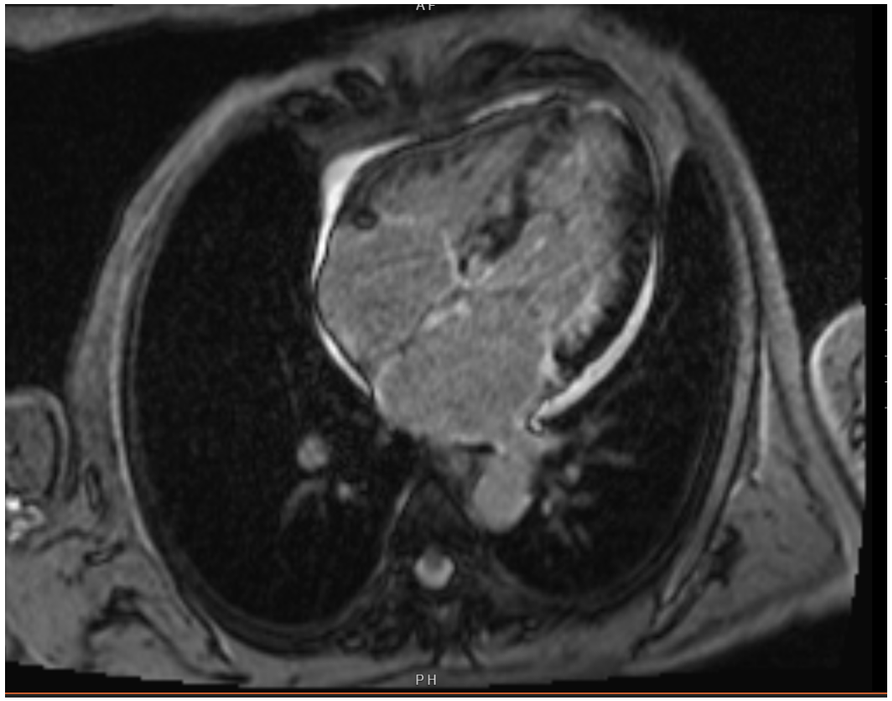


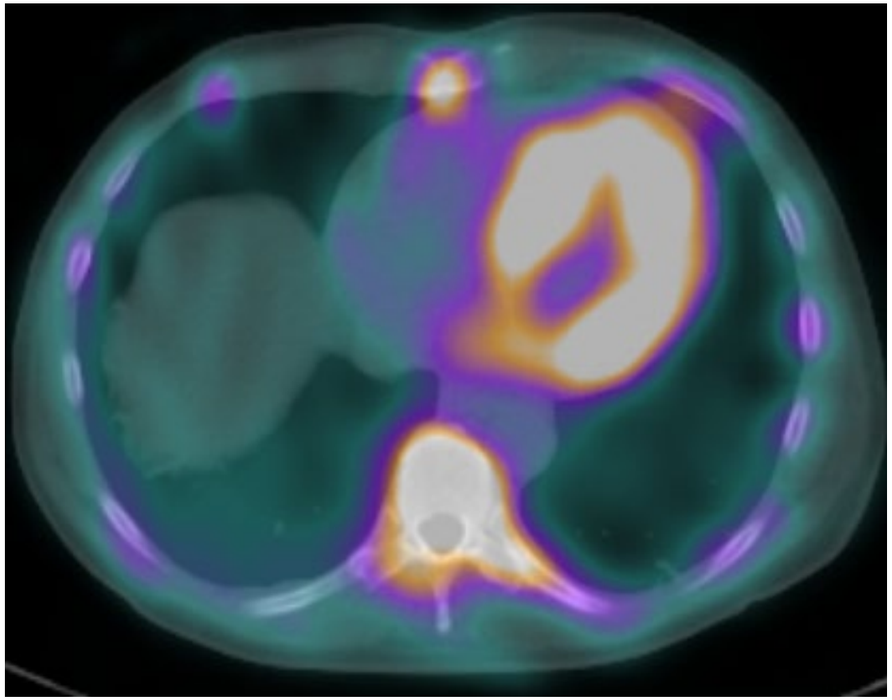
Writing Committee, Kittleson MM et al. *J Am Coll Cardiol*. 2023;81(11):1076-1126.

CASE CONTINUED

- Monoclonal profile showed a kappa/lambda ratio of 2.3 without abnormalities on immunofixation. This was felt to be expected in the setting of his diagnosis of CLL.
- Genetic testing was positive for a pathogenic mutation of the TTR gene (p.P44S).

CASE CONTINUED





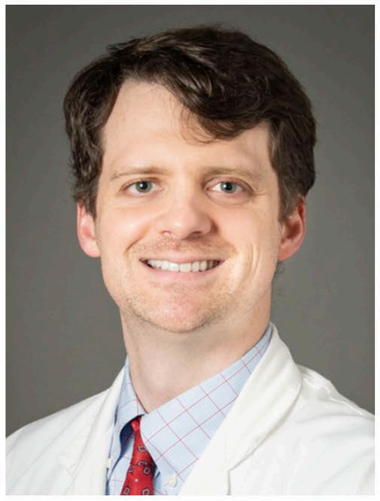
- An endomyocardial biopsy revealed focal myocardial interstitial and microvascular amyloid deposition with positive Congo red staining.
- Mass spectrometry confirmed ATTR-type amyloid deposition.

CASE CONTINUED

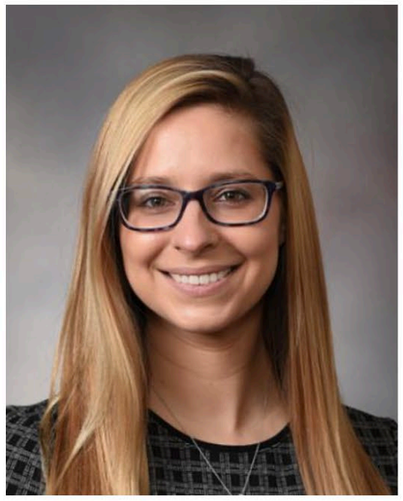
- After shared decision making discussion, he was started on TTR stabilizer therapy.
- For symptomatic LVOT obstruction, beta blocker therapy was initiated with good effect.



Sonu Abraham, MD
Director, Infiltrative Cardiomyopathy Clinic



Isaac Rhea, MD
Cardio-oncology



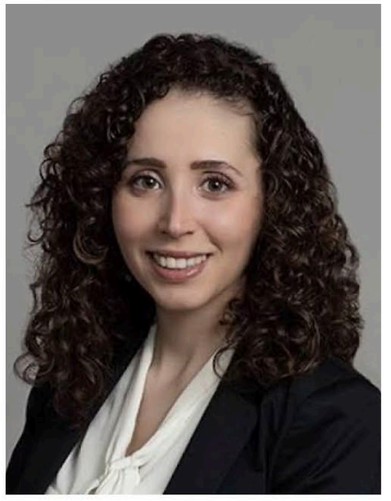
Maya Ignaszewski, MD
Advanced Heart Failure and Transplant Cardiology



Paul Anaya, MD
Critical Care Cardiology



Gregory Monohan, MD
Hematology & Oncology



Zena Chahine, MD
Hematology & Oncology

UK HealthCare

Amyloidosis Multidisciplinary Team



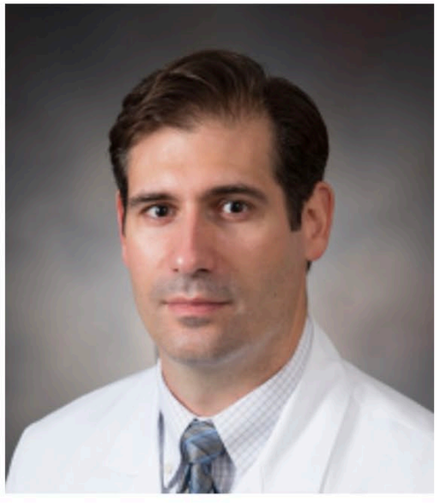
Nakul Katyal, MD
Neurology



Taha Ayach, MD
Onco-nephrology



Omar Osman, MD
Onco-nephrology



Juan-Carlos Aycinena, MD
Onco-nephrology

HealthCare

GILL HEART & VASCULAR INSTITUTE
Network

THANK YOU FOR ATTENDING THIS SESSION!

Questions/Discussion

Connecting the Heart of Kentucky

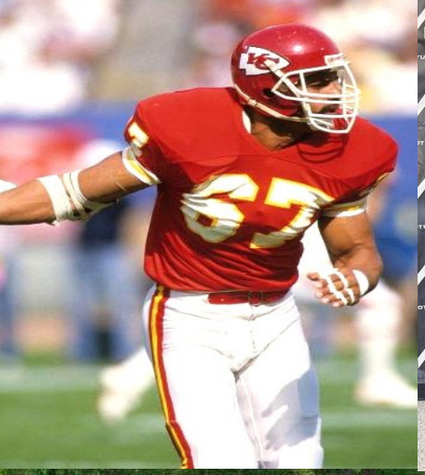
HealthCare

GILL HEART & VASCULAR INSTITUTE
Network

2026 GILL AFFILIATE NETWORK ANNUAL CONFERENCE

November 10, 2026

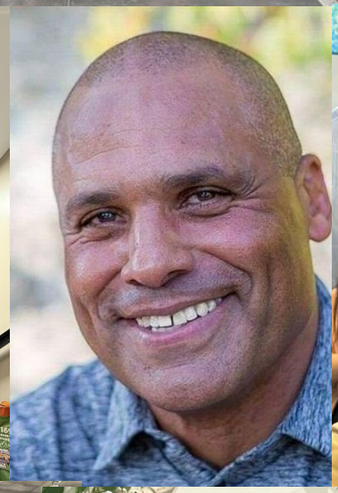
Connecting the Heart of Kentucky



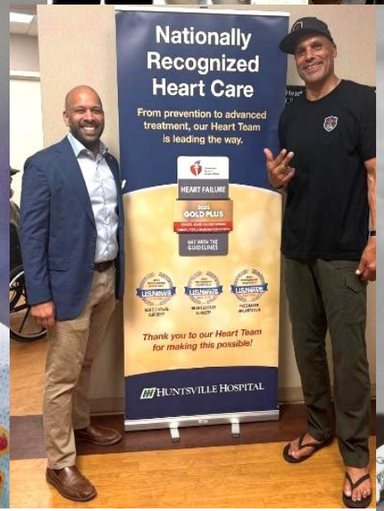
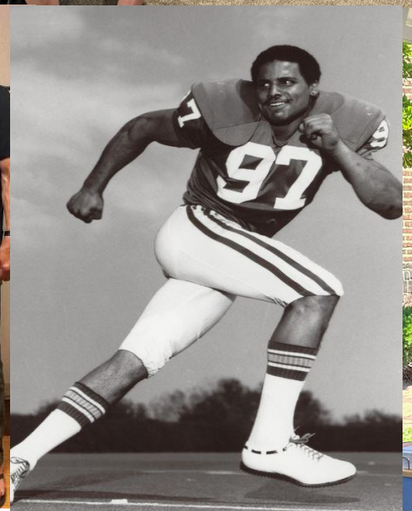



97





MEDIA


Nationally Recognized Heart Care
From prevention to advanced treatment, our Heart Team is leading the way.
HEART FAILURE
GOLD PLUS
Thank you to our Heart Team for making this possible!
HUNTSVILLE HOSPITAL

97


KCU
KCU
KANSAS CITY
