



## The Safety Net: Post-Diagnostic Monitoring of Patients With ATTR CLINICAL COMPANION TOOL

### Key Concepts for Monitoring

- Prognostic staging systems were developed in the pretreatment era and have limited value since treatments have become available
- Assess disease progression holistically using patient characteristics, biomarkers, and imaging
- Combination of NT-proBNP progression and outpatient diuretic intensification indicates worsening patient condition<sup>1</sup>
- Atrial fibrillation occurs in up to 70% of patients with cardiac amyloidosis (ATTR-CM) and ablation is associated with reduced mortality, particularly earlier in the disease process<sup>2</sup>
- Cardiac MRI (CMR) can provide comprehensive, quantitative information about myocardial structure and function to monitor response to treatment and disease progression<sup>3</sup>
- Stepwise treatment with available therapies and newer ones as they become available is often necessary to prolong survival and quality of life<sup>4</sup>
- Heart transplantation is an option as part of a comprehensive care plan and is often combined with liver or stem cell transplantation<sup>5</sup>
- Better therapies may preclude the need for transplantation<sup>7</sup>

---

### Assessing Disease Progression: Patient Characteristics

- New York Heart Association (NYHA) Class (I-IV) plus the diuretic dose in mg/kg Lasix equivalent
  - The higher the dose of diuretic, the sicker the patient
- Functional capacity measured by the 6-minute walk test (6MWT)—lower 6MWT times are associated with higher risk of mortality<sup>1</sup>
- Diuretic dose and outpatient diuretic dose intensification (ODT)
- Any recent hospitalizations or visits to urgent care
- Arrhythmias



## The Safety Net: Post-Diagnostic Monitoring of Patients With ATTR CLINICAL COMPANION TOOL

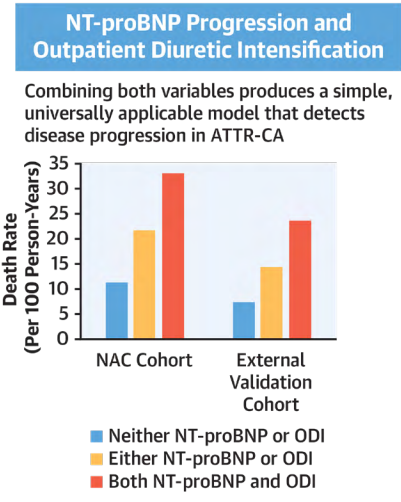
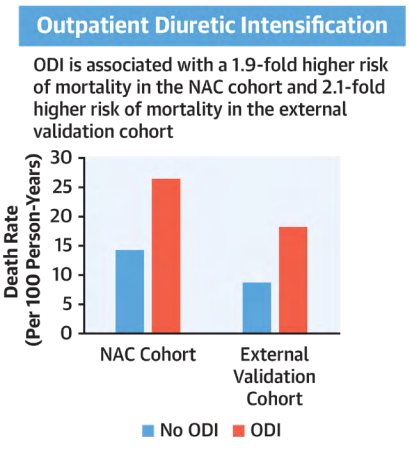
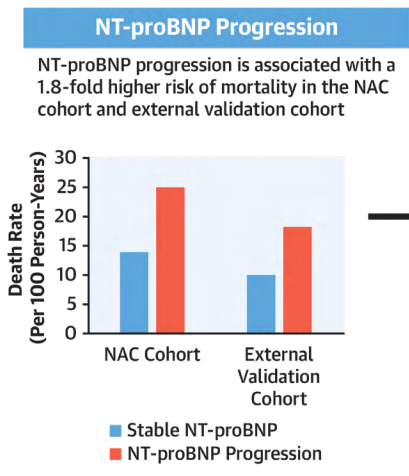
### Assessing Disease Progression: Biomarkers

#### NTproBNP<sup>1</sup>

- Can be a marker of mortality risk
- Looks at trends over time since value can fluctuate in response to external factors
- In combination with ODT, can detect disease progression

#### Prealbumin (transthyretin)<sup>8</sup>

- Normal 20-43 mg/dL
- Increases with agents such as tafamidis that stabilize the transthyretin tetramer
- Decreases with agents that silence the transthyretin gene/mRNA or deplete the ATTR protein

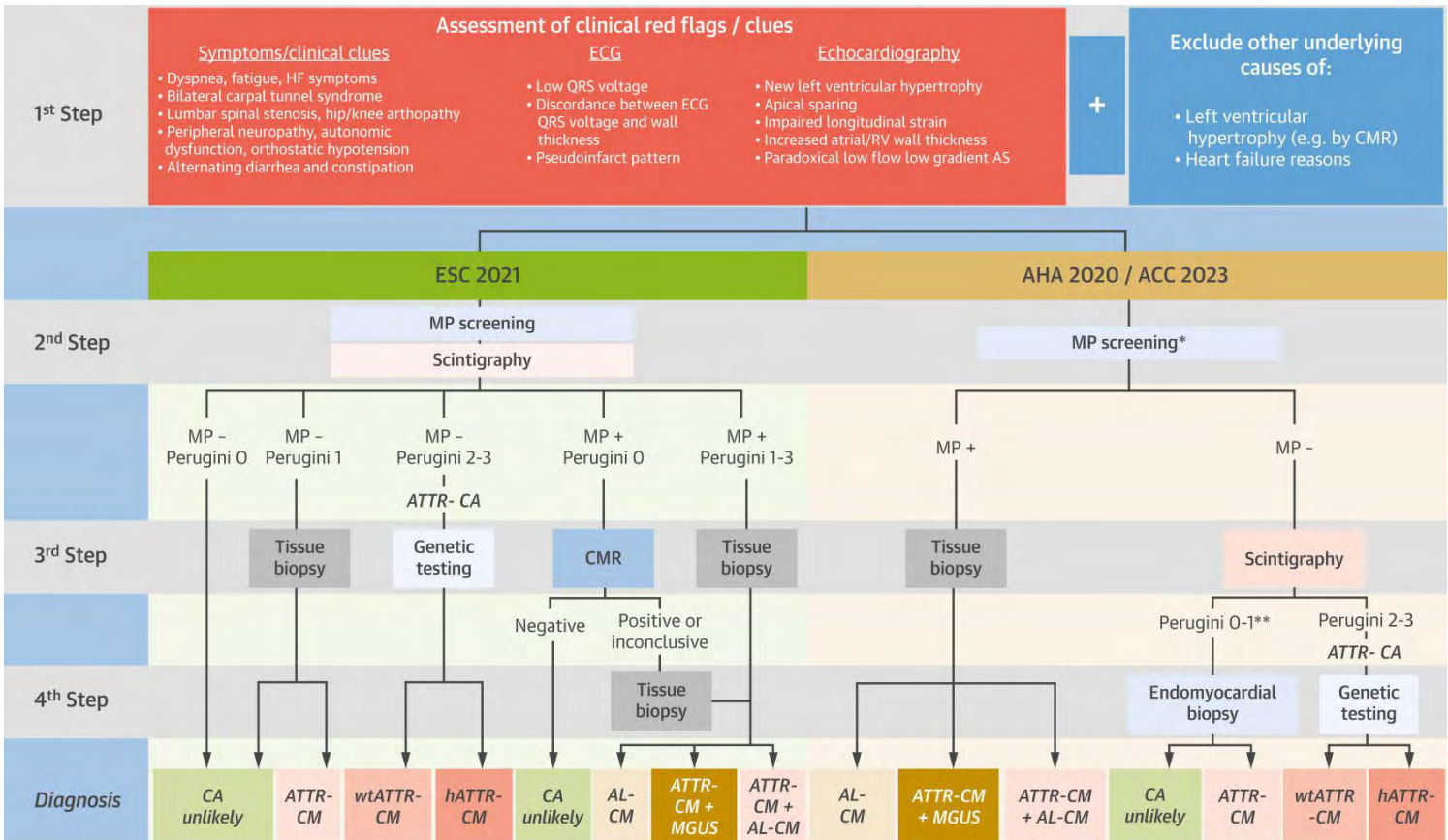


## The Safety Net: Post-Diagnostic Monitoring of Patients With ATTR CLINICAL COMPANION TOOL

### Assessing Disease Progression: Imaging<sup>1,3</sup>

- CMR plays an important role in characterizing the extent of disease in cardiac amyloidosis, which has important prognostic implications
- CMR enables precise quantitative measurements to assess interval regression vs. progression of cardiac and multi-organ amyloidosis deposition
- With multiple therapeutics on the horizon, CMR may emerge as an important imaging modality to enable patient-specific treatment selection and treatment response





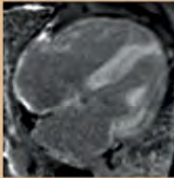
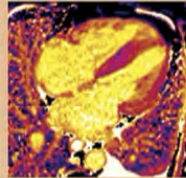
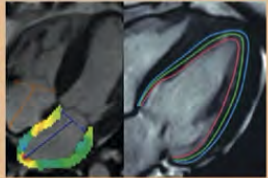
### Diagnostic Imaging Algorithm<sup>3</sup>



## The Safety Net: Post-Diagnostic Monitoring of Patients With ATTR CLINICAL COMPANION TOOL

### Multimodal Cardiac Imaging <sup>3</sup>

#### Association of Diagnostic Signs of ATTR-CM With Outcome

Bone Scintigraphy /PET	Echocardiography		Cardiac Magnetic Resonance			
						
	<b>Echo-specific parameter</b>	<b>Cine imaging</b>	<b>Late gadolinium enhancement</b>	<b>Parametric mapping</b>	<b>Segmental, RV, and atrial feature tracking</b>	
<ul style="list-style-type: none"> <li>✓ Apical sparing*</li> <li>✓ H/CL ratio ≥1.6†</li> <li>? Cardiac tracer uptake (semiquantitative)</li> <li>? Quantitative (SUV<sub>max</sub>)</li> <li>? Novel PET tracers</li> </ul>	<ul style="list-style-type: none"> <li>✓ Low GLS, abnormal E/e', right atrial area index, severe aortic stenosis‡</li> <li>✓ TAPSE§</li> <li>✓ Tissue Doppler (E/e')§</li> <li>? RELAPS, SAB, EFSR</li> <li>? Granular sparkling</li> </ul>	<ul style="list-style-type: none"> <li>✓ Thickened myocardium/LV mass§</li> <li>✓ Systolic function‡</li> <li>✓ Stroke volume§</li> <li>✓ GLS‡</li> <li>? Apical sparing</li> <li>? Thickened atrial septum</li> <li>? Torsion/twist</li> <li>? Dilated atria</li> <li>? Pericardial/pleural effusion</li> </ul>	<ul style="list-style-type: none"> <li>✓ LGE in LV  </li> <li>? LGE in RV</li> <li>? LGE in LA/RA</li> <li>? LGE extent</li> </ul>	<ul style="list-style-type: none"> <li>✓ Native T1 map¶</li> <li>✓ ECV#</li> </ul>	<ul style="list-style-type: none"> <li>? Atrial strain</li> <li>? RV strain</li> <li>? Layer strain</li> <li>? Segmental strain</li> </ul>	

✓ Association With Outcome ? Unknown Association With Outcome



## The Safety Net: Post-Diagnostic Monitoring of Patients With ATTR CLINICAL COMPANION TOOL

### Set Patient Expectations

- Select patients for treatment with tafamidis carefully<sup>9</sup>
  - Tafamidis has survival benefit over placebo
  - Good candidates
    - » Both wtATTR and hATTR
    - » NYHA stages I to III
    - » Intraventricular septum (IVS) > 12 mm
  - Not good candidates
    - » NYHA IV with low ejection fraction (EF)
    - » Advanced chronic kidney disease (CKD)
    - » Very high NT-proBNPz
- Set expectations for outcomes—even with treatment<sup>9</sup>
  - Disease will progress—tafamidis stabilizes and slows progression
  - Existing tissue or organ damage is not reversed with tafamidis
  - 6-minute walk test scores will decrease over time but in clinical trials, the decline was less with tafamidis than with placebo
  - Echocardiogram will not get better, but outcomes are better than with placebo<sup>10</sup>
- By using all available treatments, new treatments as they become available, and through participation in clinical trials, the overall survival rates are increasing
- Patients are being diagnosed earlier and at all disease stages (early, mid, and late). With various treatments and monitoring, the prognosis is better than it used to be<sup>4</sup>

### References

1. Ioannou A, Cappelli F, Emdin M, et al. [Stratifying disease progression in patients with cardiac ATTR amyloidosis](#). *J Am Coll Cardiol*. Published online March 1, 2024. doi:10.1016/j.jacc.2023.12.036.
2. Donnellan E, Wazni O, Kanj M, et al. [Atrial fibrillation ablation in patients with transthyretin cardiac amyloidosis](#). *Europace*. 2020;22(2):259-264.
3. Alwan L, Benz DC, Cuddy SAM, et al. [Current and evolving multimodality cardiac imaging in managing transthyretin amyloid cardiomyopathy](#). *JACC Cardiovasc Imaging*. 2024;17(2):195-211.
4. Martyn T, Rubio AC, Estep JD, Hanna M. [Opportunities for earlier diagnosis and treatment of cardiac amyloidosis](#). *Methodist Debaquey Cardiovasc J*. 2022;18(5):27-39.
5. Dubrey SW, Burke MM, Khaghani A, Hawkins PN, Yacoub MH, Banner NR. [Long term results of heart transplantation in patients with amyloid heart disease](#). *Heart*. 2001;85(2):202-207.
6. Estep JD, Bhimaraj A, Cordero-Reyes AM, Bruckner B, Loebe M, Torre-Amione G. [Heart transplantation and end-stage cardiac amyloidosis: a review and approach to evaluation and management](#). *Methodist Debaquey Cardiovasc J*. 2012;8(3):8-16.
7. Razvi Y, Porcari A, Di Nora C, et al. [Cardiac transplantation in transthyretin amyloid cardiomyopathy: Outcomes from three decades of tertiary center experience](#). *Front Cardiovasc Med*. 2023;9:1075806. Published 2023 Jan 19.
8. Ruberg FL, Grogan M, Hanna M, Kelly JW, Maurer MS. [Transthyretin Amyloid Cardiomyopathy: JACC State-of-the-Art Review](#). *J Am Coll Cardiol*. 2019;73(22):2872-2891.
9. Maurer MS, Schwartz JH, Gundapaneni B, et al. [Tafamidis treatment for patients with transthyretin amyloid cardiomyopathy](#). *N Engl J Med*. 2018;379(11):1007-1016.
10. Shah SJ, Fine N, Garcia-Pavia P, et al. [Effect of tafamidis on cardiac function in patients with transthyretin amyloid cardiomyopathy: a post hoc analysis of the ATTR-ACT randomized clinical trial](#). *JAMA Cardiol*. 2024;9(1):25-34.