Cleveland Clinic
Sydell and Arnold Miller Family
Heart, Vascular and Thoracic Institute

# Tall Rounds®

*Fast-paced, case-based online learning with the No. 1 hospital for heart care. Complimentary CME credit available.*

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## The Rescue: Treating Confirmed ATTR

### CLINICAL COMPANION TOOL

## Key Concepts for Treatment

- Treatment combines supportive care for cardiac amyloidosis (CA), often in conjunction with other medical specialties to manage extracardiac manifestations, and disease-modifying/targeted therapies that are approved or in clinical trials[1]
- A multidisciplinary team and network approach to care ensures the best outcomes for patients
- Tafamidis and acoramidis are FDA-approved transthyretin stabilizers to treat ATTR-CM
- The treatment paradigm is shifting from reduction to removal of amyloid deposits
- Several therapies are in development, including antibodies that can remove amyloid deposits, and your patient may benefit from participation in a clinical trial
- Earlier treatment initiation, combined with appropriate patient selection and expectations, ensures better outcomes

## Cardiac Amyloidosis

### Targets of therapy

| | Block Protein Synthesis | Stabilize Tetramer | Remove Fibrils |
|---|---|---|---|
| **Mechanism of Action** | • Gene silencing using small interfering RNA (siRNA) or antisense oligonucleotides<br>• Gene editing using CRISPR Cas 9 | Stabilizes the tetramer, thereby reducing the availability of monomers for amyloidogenesis | Antibody-mediated phagocytosis removes ATTR amyloid deposits |
| **Therapies: Approved and In Development** | **siRNA**<br>• Patisiran*[2]<br>• Vutrisiran*[3]<br>**Antisense**<br>• Inotersen*[4]<br>• Eplontersen*[5]<br>**CRISPR Cas 9**<br>• NTLA-2001[6] | • Tafamidis**[7]<br>• Diflusinal[8]<br>• Acoramidis**[6] | • NNC6019[10]<br>• NI1006 (ALXN2220)[11,12]<br>• AT-02[13] |

*FDA-approved for ATTR-PN; **FDA-approved for ATTR-CM

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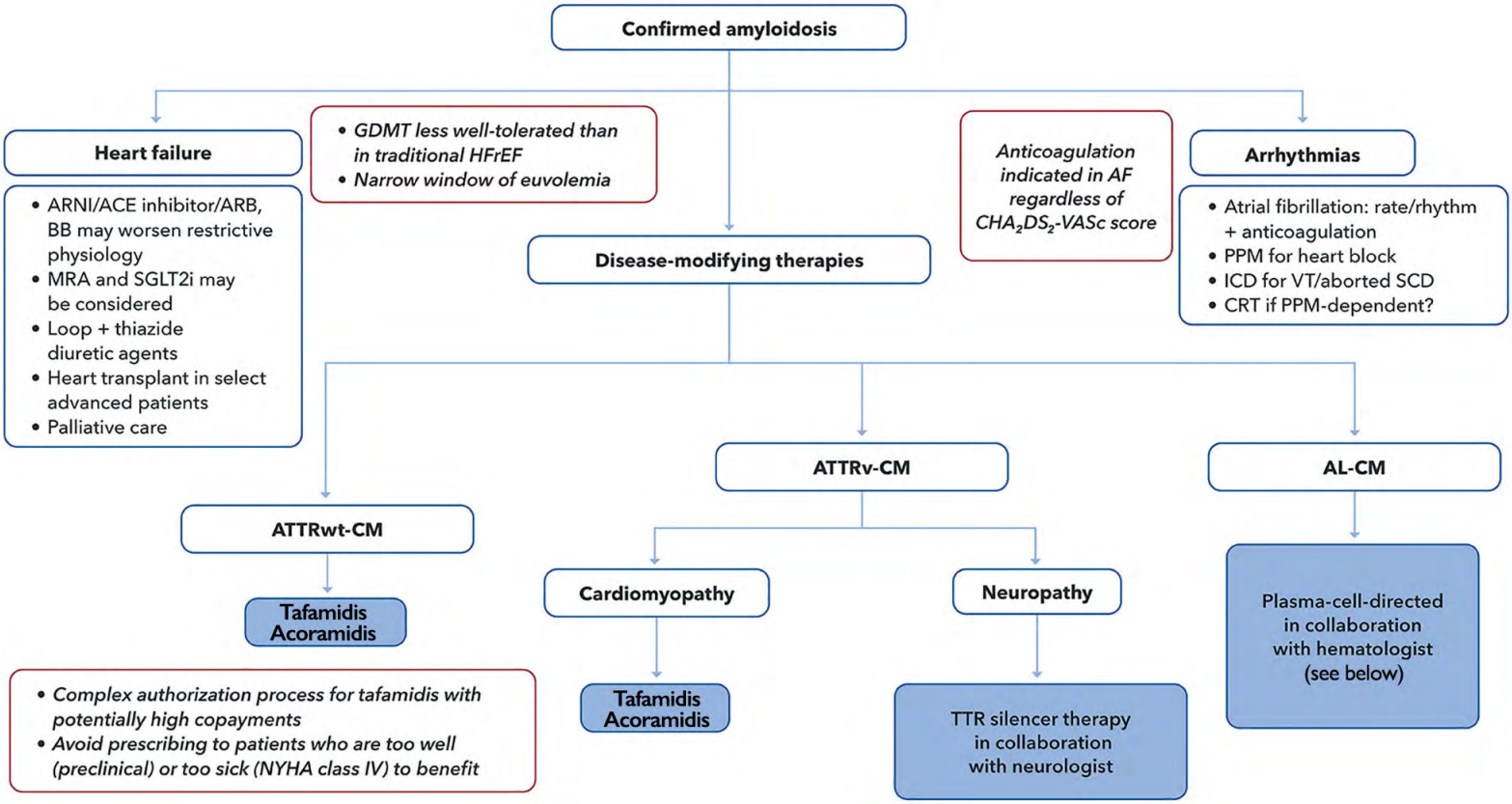
### Management algorithm[1]




AF, atrial fibrillation; ARNI/ACE inhibitor/ARB, renin-angiotensin system inhibitors; AL-CM, amyloid monoclonal immunoglobulin light chain; ATTR, amyloid transthyretin; ATTRv-CM, variant transthyretin amyloid cardiomyopathy; ATTRwt-CM, wild-type transthyretin amyloid cardiomyopathy; BB, beta-blocker; CRT, cardiac resynchronization therapy; HFrEF, heart failure with reduced ejection fraction; GDMT, guideline-directed medical therapy; ICD, implantable cardioverter-defibrillator; MRA, mineralocorticoid receptor antagonists; NYHA, New York Heart Association; PPM, permanent pacemaker; SCD, sudden cardiac death; SGLT2i, sodium glucose cotransporter 2 inhibitor; TTR, transthyretin; VT, ventricular tachycardia.



# The Rescue: Treating Confirmed ATTR

## CLINICAL COMPANION TOOL

## AL Amyloidosis

Light chain amyloidosis (AL) most commonly results from clonal plasma cell disorder and, therefore, treatments include chemotherapy and immunotherapy agents similar to those used for myeloma.

### Targets of therapy[14,15]

#### Therapies approved and in development:

| Reduction in Light Chain Production | Inhibition of Amyloid Fibril Formation | Removal of Light Chain Amyloid Deposits |
|---|---|---|
| • Bortezomib<br>• Carfilzomib<br>• Daratumumab<br>• Elotuzumab<br>• Isatuximab<br>• Ixazomib<br>• Lenalidomide<br>• Pomalidomide<br>• Venetoclax | • Doxycycline | Anti-fibril antibodies<br>• Anselamimab (CAEL-101)<br>• Birtamimab |

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## CLINICAL COMPANION TOOL

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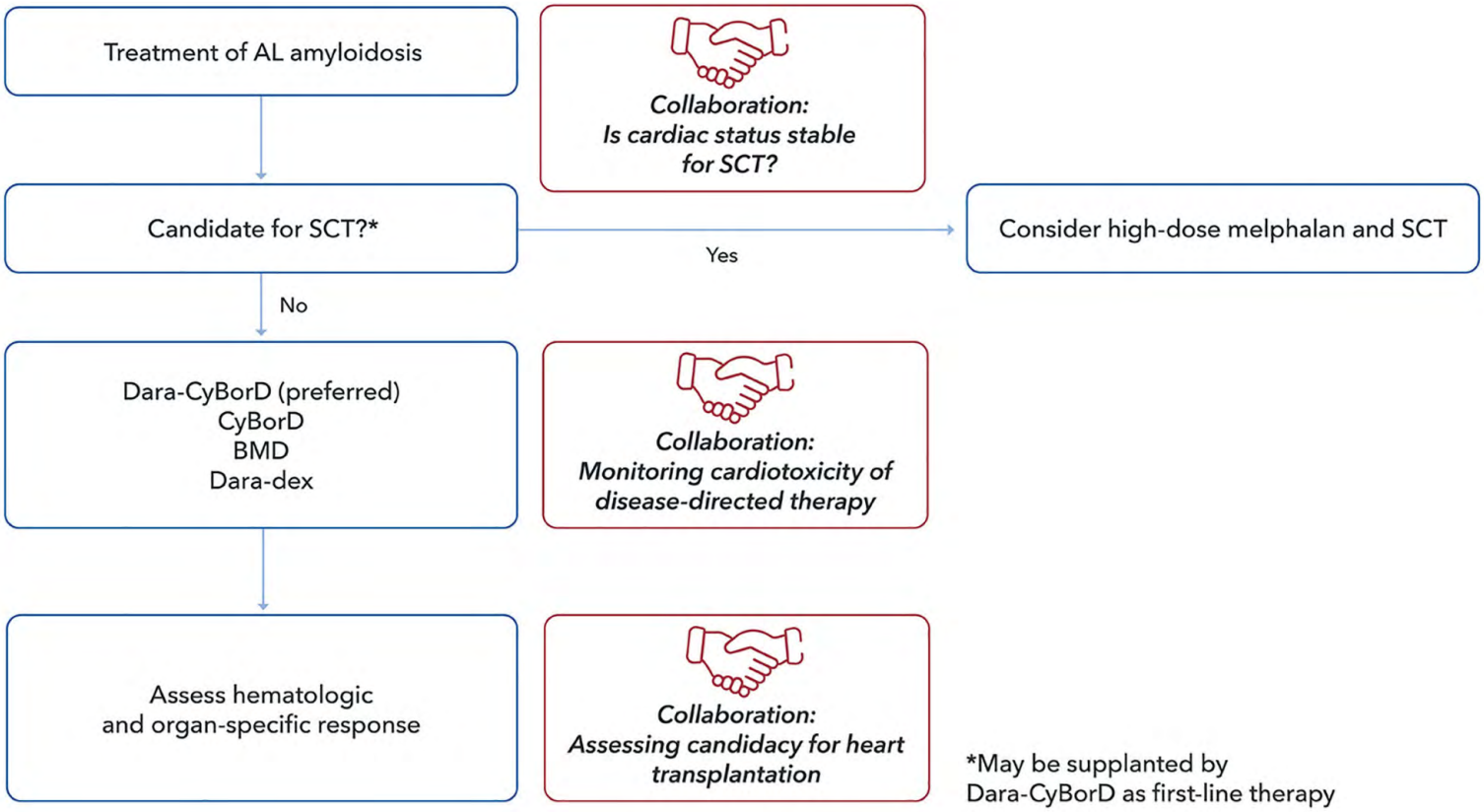


AL, light-chain amyloidosis; BMD, bortezomib-melphalan-dexamethasone; CyBorD, cyclophosphamide, bortezomib, and dexamethasone; Dara, daratumumab; dex, dexamethasone; SCT, stem cell transplantation



# The Rescue: Treating Confirmed ATTR

## CLINICAL COMPANION TOOL

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