**MHIF FEATURED STUDY:**

**NanoCor**

**DESCRIPTION:** an early phase, non-randomized study evaluating the safety of a single antegrade epicardial coronary artery infusion of NAN-101 in up to 12 subjects with non-ischemic cardiomyopathy and NYHA class III symptoms.

NAN-101 is a gene therapy product composed of a novel adeno-associated virus designed to target cardiomyocytes and deliver its payload of I-1c transgene. This genetic material provides code for an upstream inhibitor of the SERC2a pathway, which has been identified as a primary pathogenic mechanism in heart failure. The goal is to improve calcium cycling within the heart.

Preclinical studies have shown that constitutively activating I-1 within the failing rat heart improved not only contractility, but also reversed adverse remodeling by directly decreasing fibrosis and cardiac hypertrophy.

**CRITERIA LIST/QUALIFICATIONS:**

**Inclusion:**
- Chronic non-ischemic cardiomyopathy
- LVEF of 30% or less
- NYHA III

**Exclusion:**
- Ischemic cardiomyopathy
- Restrictive cardiomyopathy/ infiltrative cardiomyopathy
- Renal failure

**CONDITION:**
Non-Ischemic Cardiomyopathy

**PI:**
Jay Traverse, MD
Kasia Hryniewicz, MD

**RESEARCH CONTACTS:**
Jake Jensen – Jacob.Jensen@allina.com | 612-863-3818
Kari Thomas - Kari.M.Thomas@allina.com | 612-863-7493

**SPONSOR:**
AskBio

Currently Enrolling

EPIC message to Research MHIF Patient Referral

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MHIF Cardiovascular Grand Rounds | February 8, 2021
MHIF FEATURED STUDY: SOLVE-CRT
Stimulation Of the Left Ventricular Endocardium for Cardiac Resynchronization Therapy in Non-Responders, Previously Untreatable and High-risk Upgrade Patients

| CONDITION: | PI: Jay Sengupta, MD | RESEARCH CONTACT: Jessie Whelan | SPONSOR: EBR Systems |
| Heart Failure with previously untreatable CRT or High-Risk Upgrades (HRU)* |

DESCRIPTION:
Three-part study that will work to demonstrate the safety and effectiveness of the WiSE CRT System. Two-part procedure (first implanting transmitter and battery and then implanting electrode in LV) followed by 5-year follow-up.

CRITERIA LIST/QUALIFICATIONS:

**Inclusion:**
- Patient with a class I or IIa indication for implantation of a CRT device and one of the following:
  - CRT non-responder
  - EF remained unchanged or worsened since implant **AND**
  - Patient’s clinical status has remained unchanged or worsened
  - Previously untreatable patient because CRT failed or programmed off
  - High-Risk Upgrade
- Patient is on stable Guideline Directed Medical Therapy
- Patient has suitable anatomy for implant
  - Adequate acoustic window, LV wall thickness in implant area >5mm, and absence of LV wall structural abnormalities)

**Exclusion:** (partial list)
- Pure RBBB
- LVEDD > 8 cm
- Non-ambulatory or unstable NYHA class IV
- Contraindications to heparin, chronic anticoagulants, or antiplatelet agents
- AF patients with RV pacing < 95% and/or have documented AF episode > 30 minutes or cardioversion within last 30 days
- Patients with prosthetic AV and non-viable transeptal approach, or patients with prosthetic MV and non-viable aortic approach for implant

*About 30% of patients have been found to not respond clinically to CRT.*
MHIF FEATURED STUDY:
Myocardial perfusion and contraction assessed by cardiac MRI in acute and recovery takotsubo syndrome

OPEN AND ENROLLING / EPIC message: Research MHIF Patient Referral

CONDITION: Takotsubo syndrome (TS)

PI: Retu Saxena, MD
Co-I: Scott Sharkey, MD

RESEARCH CONTACTS:
Steph Ebnet
stephanie.ebnet@allina.com | 320-291-8950
Sarah Schwager
sarah.schwager@allina.com | 319-350-9643

SPONSOR: MHIF IIR

DESCRIPTION: This study will use the new respiratory motion-corrected automated in-line perfusion mapping stress CMR protocol to quantify regional myocardial blood flow (MBF) and myocardial perfusion reserve (MPR) in TS patients resulting in a “myocardial perfusion map” which can be correlated with a “myocardial contraction map.”

CRITERIA LIST/ QUALIFICATIONS:

Exclusion:
- Significant acute or chronic renal disease (dialysis or estimated glomerular filtration rate <30 ml/min/m2)
- Contraindication to adenosine or gadolinium
- Decompensated acute heart failure (need for mechanical ventilation, vasopressor treatment of hypotension, mechanical circulatory support)
- Pregnancy or lactation
- Atrial fibrillation or sustained ventricular tachycardia/ventricular fibrillation
- Asthma requiring hospitalization or oxygen dependent COPD
- Bradycardia or advanced heart block unless pacemaker present

Inclusion:
- Admitted with acute TS without significant coronary artery obstruction as defined on invasive coronary angiogram or CT coronary angiogram
- Typical apical or mid-ventricular ballooning pattern based on initial echocardiogram or left ventriculogram
- Age > 18 years
2020 EP review for the non-EP

KRISTOPHER D KRUEGER, MD, PHD
CARDIAC ELECTROPHYSIOLOGIST

No Disclosures
My introduction to some at MHI:

Methods/Objectives

- Review of "important" articles from 2020
  - Purely subjective.
  - Avoided articles focusing on technical EP topics.
  - No COVID related articles.
- Objectives:
  - Identify advances and potential advances for implantable devices.
  - Identify limits in monitoring tech.
  - List some newer data on atrial fibrillation topics.
Atrioventricular Synchronous Pacing Using a Leadless Ventricular Pacemaker


- Built off Marvel study (Chinitz et al., Heart Rhythm, 2018; 15: 1363-1371).
  - 64 patients (33 with high degree AV block).
  - Accelerometer-based atrial sensing is feasible and improves AVS.
- 75 patients from 12 centers. 40 had predominantly SR with CHB.
- Downloaded accelerometer-based algorithm.
- Primary efficacy objective was to demonstrate superiority of algorithm to provide AV synchronous (VDD) pacing versus VVI-50 pacing (SR with CHB).
- Safety endpoint: no pauses or heart rates of >100 bpm.
How does algorithm work? Sensing Vectors

ACCELEROMETER CAN DETECT MECHANICAL ACTIVITY: ACCELEROMETER SIGNALS CORRESPOND TO HEART SOUND TIMING & KNOWN CARDIAC ACTIVITY

Vector 2 (longitudinal) best overall for picking up the atrial kick (A4)
NOTE THAT ACCELEROMETER SIGNALS CORRESPOND TO HEART SOUND TIMING & KNOWN CARDIAC ACTIVITY

AV Synchronous Pacing %

- Mean AV synchrony pacing % from 26.8% → 89.2% with VDD pacing.
- 94.3% median AV synchrony at rest.
- 95% of patients (38/40) had ≥70% AV synchrony.
- 8.8% improvement in SV (based on LVOT VTI).
Variable Response to Algorithm

- Bottom tile shows no response but some degree of “AV synchrony”
  - Some pts have periods of AV synchrony.
  - Some P waves fortuitously fall just before V pacing.
- Garweg et al., Heart Rhythm, 2020; 17: 2037-2045.
  - Looked at 64 patients in MARVEL 2 with visible P waves.
  - High AVS = good A4 signal (good atrial mechanical function).
  - Predictors of good A4 signal amplitude
    - E/A ratio <0.94
    - Low sinus rate variability.

Appropriate Micra AV Patients

- Lack of atrial pacing indications.
- Infrequent pacing.
- Vascular access issues.
- Sedentary patients.
- Other comorbidities.
Current and Planned CRM Studies at MHI

- **EV-ICD**: Subcutaneous ICD
  - **PI**: Dr. Gornick

- **SOLVE-CRT**: Endocardial LV pacing
  - **PIs**: Dr. Moore and Dr. Sengupta

- **LEADR**: 4FR ICD lead.
  - **PI**: Dr. Zakaib

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Implantable Loop Recorders
Incidence of false (+) transmissions during remote monitoring with ILRs

- 695 remote transmissions on 559 pts over 4 weeks
  - AF surveillance: 321
  - Cryptogenic stroke: 168
  - Syncope: 70
- Primary reason for FP:
  - Scheduled: signal dropout and undersensing.
  - Alert: ectopy.
- ADJUDICATION!!!
  - 30-45 min for device RN+EP

ILR False positive

70 y/o female admitted to ANW hospital on 12/9/2020.
- Left sided facial droop and worsening upper/lower extremity weakness.
- CTA with occlusion at origin of M2 branch of right MCA
- Outside of tPA window and not a mechanical thrombectomy candidate.
- ILR placement on 12/11/2020 for CS.
“It all started when I got my Apple Watch.”

Wearables:
- Market of 27.49 billion in 2026.
- 9% in 2014 → 33% in 2018.
- By 2022: estimated 67 million users in US.

Dagher et al., Heart Rhythm, 2020; 17: 889.

Table 5
Summary of validity, representing sensitivity and specificity of eligible studies.

<table>
<thead>
<tr>
<th>Research</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chan et al[12]</td>
<td>75% (95% CI 70–80%)</td>
<td>98.2% (95% CI 59.3–70.5)</td>
</tr>
<tr>
<td>Desteghe et al[13]</td>
<td>54.5%–78.9%</td>
<td>97.5%–97.9%</td>
</tr>
<tr>
<td>Evans et al[14]</td>
<td>Unreported</td>
<td>Unreported</td>
</tr>
<tr>
<td>Halcox et al[15]</td>
<td>Unreported</td>
<td>Unreported</td>
</tr>
<tr>
<td>Lown et al[16]</td>
<td>87.8% (95% CI 78.7–93.9%)</td>
<td>98.6% (95% CI 96.3–99.6%)</td>
</tr>
<tr>
<td>Lowres et al[17]</td>
<td>98.5%</td>
<td>91.4%</td>
</tr>
<tr>
<td>Lowres et al[18]</td>
<td>94.6% (95% CI, 85.1–98.9)</td>
<td>92.9% (95% CI, 92.0–93.8)</td>
</tr>
<tr>
<td>Soni et al[19]</td>
<td>Unreported</td>
<td>Unreported</td>
</tr>
<tr>
<td>Soni et al[20]</td>
<td>Unreported</td>
<td>Unreported</td>
</tr>
<tr>
<td>Tarakji et al[21]</td>
<td>100%</td>
<td>97%</td>
</tr>
</tbody>
</table>

CI = confidence interval.

Effectiveness of AliveCor (Kardia mobile) device for AF screening
Hall et al., Medicine, 2020; 99: 30
- Rates of AF detection: 0.8-36%
- Rather good.
- Does not pick everything up and may still be wrong: patient education!
Wearable Accuracy in SVT

- Device placed on wrist during EPS for SVT on 52 patients.
- All devices inaccurate at HR detection of short SVT.
- If an elevated heart rate is detected, it is likely real.
- Some devices are accurate at detecting elevated HRs during longer SVT.

Topics in Atrial Fibrillation
Reduced Risk of Dementia/CI with OAC for AF

- Retrospective cohort study.
- 84521 with AF
  - 35245 on OAC
  - 49276 not
- 10% lower risk in patients on OAC versus not.
- No difference in warfarin vs DOACs
- Increased risk of dementia in patients on OAC/antiplatelet Rx

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Count</th>
<th>Hazard Ratio</th>
<th>Effect_size</th>
<th>P_interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure</td>
<td>7702</td>
<td>0.86 (0.72-1.05)</td>
<td>0.179</td>
<td></td>
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<tr>
<td>Hypertension</td>
<td>7523</td>
<td>0.87 (0.72-1.06)</td>
<td>0.1147</td>
<td></td>
</tr>
<tr>
<td>Age &gt; 75 or more than 75 years</td>
<td>4200</td>
<td>0.94 (0.83-1.00)</td>
<td>0.7317</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>8295</td>
<td>0.80 (0.68-0.96)</td>
<td>0.7791</td>
<td></td>
</tr>
<tr>
<td>Stroke/TIA/SE</td>
<td>8714</td>
<td>0.77 (0.69-0.87)</td>
<td>0.1775</td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease RX</td>
<td>8592</td>
<td>0.80 (0.68-0.96)</td>
<td>0.6631</td>
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<tr>
<td>Gender Male</td>
<td>8329</td>
<td>0.85 (0.72-0.99)</td>
<td>0.7002</td>
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</tr>
<tr>
<td>CHA2DS2-VASC score</td>
<td>8093</td>
<td>0.86 (0.79-0.96)</td>
<td>0.2196</td>
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<tr>
<td>HABIT score</td>
<td>6135</td>
<td>0.90 (0.83-0.99)</td>
<td>0.4227</td>
<td></td>
</tr>
<tr>
<td>AF treatment</td>
<td>6097</td>
<td>0.86 (0.79-0.93)</td>
<td>0.7181</td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>5759</td>
<td>0.90 (0.85-0.95)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

EtOH Moderation and AF Recurrence

- Prospective, randomized 6 hospitals in Australia, 140 patients.
- AF and 10+ EtOH drinks/week.
  - Abstinence: 16.8±7.7 → 2.1 ± 3.7 (complete: 61%)
  - Control: 16.4±6.9 → 13.2 ± 6.5
- Endpoints after 2 week blanking period
  - Freedom from AF recurrence at 6 months.
  - Abstain: 53% versus 73%
  - AF burden over 6 months.
  - Abstain: 0.5% versus 1.2%
EtOH and AF Risk in Healthy Adults  
Cha et al., Heart Rhythm, 2020; 17: 2086-2092

19634 patients 2007-2015 in South Korea
- Retrospective screening of healthy pts, no AF
- Excluded those with any medical/surgical history.
- Average follow-up: 7.0±2.8 years.
- Any EtOH use increased risk of AF.
- Highest risk was for frequent, binge drinkers.

Impact of Bariatric Surgery on AF Type  
Donnellan et al., Circulation: Arrhythmia and Electrophysiology, 2020; 13 (2): 106

- 220 Control
  - 10.1% weight loss
  - No AF reversal
- 220 underwent BS (loss%/AF reversal%)
  - Gastric bypass: 25/70
  - Sleeve gastrectomy: 19/56
  - Gastric banding: 16/50
- No benefit in long-standing or permanent AF.
Higher Cardiopulmonary Fitness Associated with Lower Recurrence after AF ablation

Donnellan et al., Heart Rhythm, 2020; 17: 1687-1693.

- 591 consecutive patients
  - Retrospective 1/2012-1/2018.
  - Undergoing ablation for AF.
  - Had exercise stress test within 12 months prior to ablation.
- 3 groups
  - Low CRF: <85% predicted METs
  - Adequate CRF: 85-100%
  - High CRF: >100%
  - Similar patient characteristics between 3 groups.
- Outcomes: mean f/u 32 months.
  - Arrhythmia recurrence: 79%, 54% and 27.5%
  - Death: 11%, 4% and 2.5%

Generalizability of CASTLE-AF Trial: Does it apply to general practice?

Noseworth et al., Heart Rhythm, 2020; 17: 1057-1065

- Large retrospective database
  - 289831 AF/HF patients
  - 7465 Rx with ablation
  - 282366 Rx with medical therapy.
  - CASTLE-AF applicable population?
    - 7.8% met CASTLE-AF eligibility
    - 91% failed inclusion criteria.
    - 15.5% failed exclusion criteria.
- Primary endpoint: composite of death and HF hospitalization.
  - 18% reduction
  - 38% reduction in CASTLE-AF.
Early Rhythm Control of Atrial Fibrillation  
Camm et al., NEJM, 2020, 383: 1305

- Randomized 2789 patients (135 centers)
  - Diagnosed within last year.
  - 75 or older, prior TIA/stroke or at least 2 criteria (CHADSVASC + CKD and LVR)
  - Median time since diagnosis: 36 days.
  - Early rhythm control (abl or AAD) versus usual care (Rx guided by symptoms)
- Primary endpoints
  - Composite of CV death, stroke or hospitalization for CHF or ACS.
  - Hospitalization days.
- Results
  - No difference in hospital days.
  - 249 versus 316 patient events favoring early rhythm control (HR: 0.79, p=0.005).

Conclusions:
- CRM: Pacing and ICD options continue to expand.
- ILR and wearable tech:
  - Adjudication of any of these results important.
  - Wearable tech options are expanding and have clear limitations.
  - Importance of patient education.
- Atrial fibrillation:
  - Multiple studies have confirmed reduction of dementia with OAC in AF.
  - Risk factor modification needs to be emphasized: EtOH, weight loss (BS) and fitness.
  - Benefit of ablation in some AF patients with CHF.
  - Early rhythm control important.