“Congestive Heart Failure Update and Management and Review of Clinical Trials”
Joyce W. Wald, DO

Disclosures
• Advisory Board
  • Medtronic
• Speaker’s Bureau
  • None
• Supported Clinical Trials
  • Medtronic
  • Abbott
  • Novartis

Today’s Agenda
• Background
  • We will be discussing SYSTOLIC heart failure: HFrEF
  • Evaluation for reversible causes
• Chronic systolic heart failure
  • Current therapies
  • New Therapies
    • Medical
    • Device
    • Clinical trials
  • How to tell a patient is failing despite treatment
• Acute systolic heart failure
  • Current and new therapies
  • Heart transplant and mechanical circulatory support
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Etiology of Cardiomyopathy

- Abnormal loading conditions
  - Valvular disease
  - Hypertension
  - Shunts
- Toxins
  - Chemotherapeutics
  - Cytokines, viral
  - Alcohol
- Genetic
  - Familial
  - Muscular dystrophies
  - Mitochondrial disorders
  - Hypertrophic
  - ARVD
  - Non-compaction cardiomyopathy
- Insults
  - Ischemia
  - Thyroid disease
  - Tachycardia
  - High PVC burden
- Unclear etiology
  - Peripartum
  - Idiopathic
  - HIV
  - Infiltrative & diastolic HF
  - Amyloidosis
  - Sarcoidosis
  - Hypertrophic
  - Idiopathic restrictive CMP
Just one family can lead to the identification of a high risk gene to help then prognosticate not only the patient, but their family members.

Cardiomyopathy evaluate for reversibility

- Alcohol intake?
  - In persons who consumed 70 g of ethanol (or the equivalent of 7oz of whiskey, 20 oz of wine, or 72 oz of beer [ie, six 12-oz cans]) per day for 20 years, 36% had an abnormal ejection fraction.
- Tachycardia mediated
- Asynchrony
- PVC-induced (≥ 10%)
- BBB
- RV pacing
- Ischemia
- Valvular disease


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Cardiomyopathy evaluate for reversibility
• When to perform endomyocardial biopsy

Lymphocytic myocarditis
Giant Cell Myocarditis

Think about myocarditis with arrhythmias, + troponin

Gotsman & Keren Fulminant lymphocytic myocarditis vs giant cell myocarditis. ESCARDIO.org Oct 2008
Yeglee N et al Value of MRI in patients with a clinical suspicion of acute myocarditis. EUR RAD 2007;17;2211

Think Sarcoid with CHF, arrhythmias
Kandolin R et al. Cir Arrhythm Electrophysiol 2011;4:303-309

Cardiomyopathy evaluate for reversibility
• When to perform endomyocardial biopsy

Cardiomyopathy evaluate for reversibility

Cardiomyopathy evaluate for reversibility

Goals of Therapy: Chronic Versus Acute HF

Long-Term Goals
- Ventricular Reverse Remodeling
- Vascular Remodeling
- Increased PCWP
- Decreased CO
- Neurohumoral Antagonists
- Hemodynamic Agents
- Vasodilators
- Inotropes
- Diuretics

Short-Term Goals
- Ambulatory, euvolemic
- Decompensated
- Relief of Symptoms
- Stabilization of Organ Function

PCWP = pulmonary capillary wedge pressure
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**First-line therapy**

**B blocker**

- Effects
  - Inhibit the adverse effects of sympathetic system
    - Delay and reverse remodeling
  - Improve survival, morbidity
  - Clinical use: systolic and diastolic heart failure
  - Given to all patients with systolic HF in absence of fluid overload
  - Adverse effects
    - Hypotension, bradycardia, worsening HF
    - Lingering questions
      - Class effect?
      - Target heart rate?
      - Target dose?

*Good review: Bristow M. Beta adrenergic blockade in chronic heart failure. Circulation 2000;101:558-69*
BB Dose Matters: almost 20 years later!!!!!!
Presented at HFSA 10/2015

Baseline Heart Rate
Low = < 70 bpm
Hi = ≥ 70 bpm

Low dose, high HI
1.3 x higher risk of bad outcome: All cause death, all cause hosp
The beneficial effect is beyond the HR effect, even if HR is already low.

Furst Fibres, Heart Rate or Beta-Blocker Dose? Association with Outcomes in Ambulatory Heart Failure Patients with Systolic Dysfunction: Results from the HF-ACTION Trial, JACC: Heart Failure (2015), doi: 10.1016/j.jchf.2015.09.002.

Secondary aldosteronism in CHF

- Two pathophysiologic mechanisms
  - Increased production by adrenals
  - Decreased hepatic clearance
- Effects of aldosterone:
  - Sodium retention
  - Potassium and magnesium loss
  - Myocardial and vascular fibrosis
  - Baroreceptor dysfunction
  - Impairs arterial compliance
  - Decreased myocardial norepinephrine uptake
Aldosterone Inhibitors

**RALES Trial**
- 1663 NYHA III-IV
- 25 mg Aldosterone vs Placebo
- 30% reduction in death*
- Progressive HF
- SCD
- 35% reduction in hospitalization
- Significant improvement in NYHA functional class

**EPHESUS Trial**
- 6632 pts, 14 d after AMI, EF < 40%
- Aldosterone vs Placebo
- 30% reduction in death*
- Progressive HF
- SCD
- 35% reduction in hospitalization
- Significant improvement in NYHA functional class

**EMPHASIS Trial:**
- N=2737 with mild HF EF < 35%
- Improvement with Epleranone

Hydralazine (target dose: 100 mg three times a day)
Isosorbide mononitrate (target dose: 40 mg three times a day)

Taylor AL, et al. NEJM 2004;351:2049-57

**A-HeFT:**

**Inclusion Criteria**
- Self-identified African American, symptomatically stable NYHA class III-IV on standard HF treatment; b-blockers for at least 3 months
- LVEF ≤ 35% or LVEF <45% and a resting LVIDD >2.9 cm/m² or >6.5 cm (by Echo)

**Exclusion Criteria**
- Women of childbearing age who were pregnant, nursing, or not using contraception
- MI, ACS, CVA, cardiac surgery, PCI within 3 months
- Valvular disease, HOCM, restrictive CMY, myocarditis
- Ventricular arrhythmias unless ICD
- Requirement for inotropes or CHF therapy

Taylor AL, et al. NEJM 2004;351:2049-57

**A-HeFT: 43% Relative Risk Reduction for Mortality**
ARNI: valsartan/sacubitril (LCZ696)*
Sinoatrial node modulator: ivabradine**

*PARADIGM-HF 2014;371:993 NEJM
**SHIFT 2010;376:875 Lancet

N = 8442 NYHA II, - IV HF EF < 40% LCZ696 200 mg BID vs enalapril 10 mg bid.

FDA approval but await long term OC

Angiotensin–Neprilysin Inhibition in Acute Decompensated Heart Failure

POMA 111th Annual Clinical Assembly
May 1-4, 2019
Incorporating Sacubitril/Valsalnt into practice

- PARADIGM-HF Trial enrolled mostly NYHA Class II and some Class III ambulatory patients.
- May be limited by blood pressure in patients with more advanced disease.
- Incorporates in lieu of an ACE or ARB for Stage C with NYHA Class 2 or 3 symptoms without significant renal insufficiency or hyperkalemia.
- PIONEER-HF suggests that Sacubitril/Valsalnt can be started during acute heart failure hospitalization without harm, and biomarker evidence of improving BNP (short term study 8 weeks).
- WATCH RENAL FUNCTION CAREFULLY.

PARAGON-HF Trial (honorable mention)

- Randomized, double-blind, parallel group, active-controlled, event-driven trial comparing the long-term efficacy and safety of valsartan and sacubitril/valsartan in patients with chronic HFrEF (left ventricular ejection fraction ≥45%).
- NYHA II to IV symptoms.
- Elevated natriuretic peptides and evidence of structural heart disease.
- Sequential single-blind run-in periods to ensure tolerability of both drugs at half the target doses.
- The primary outcome is the composite of cardiovascular death and total (first and recurrent) HF hospitalizations.

Results due late 2019 or 2020

N=6558 ivabradine 7.5 mg bid
Vs placebo (OMM)

Ivabradine selectively inhibits the sinus node thereby decreasing myocardial oxygen demand without affecting inotropy or blood pressure.

Swedberg Lancet 2010;376:875
Inclusion Criteria Background Tx

- >18 years
- Class II to IV NYHA heart failure
- Ischaemic/non-ischaemic aetiology
- LV systolic dysfunction (EF ≤ 35%)
- Heart rate >70 bpm
- Sinus rhythm
- Documented hospital admission for worsening heart failure <12 months

Ivabradine significantly reduces major risks associated with heart failure (f/u up to 23 months):

- 18% reduction in CV death or hospital admission for worsening HF
- 26% reduction in hospital admission for worsening heart failure
- No benefit for all cause or CV mortality alone

Benefits are apparent early (within 3 months), are consistent in predefined subgroups, and have been demonstrated on top of recommended therapy. Treatment is well tolerated.

Conclusions

FDA

- On April 15, 2015 the FDA approved Ivabradine in the US
  - "To reduce the risk of heart failure hospitalization"
  - LVEF less than 35%
  - Heart rate above 70 BPM (sinus) on maximally tolerated beta blockade
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Take Away Points: ambulatory HFpEF patients
- ACE-inhibitors are still first line therapy (high dose if BB intolerant)
- ARBs is as effective if ACE intolerant, the addition of ARB to ACE therapy may be done without harm, maybe some benefit, but close watch of potassium and renal function
- Beta Blockers: dose matters, try and achieve target doses, even at the cost of vasodilator dose
  - Carvedilol 25 mg bid (US carvedilol Trial)
  - Metoprolol Succinate 150 mg daily (MERIT HF Trial)
  - Bisoprolol 7.5 mg daily (CIBIS Trial)
- We are using aldosterone inhibitors earlier, they are becoming also part of the mainstay of therapy
- Caveat: compliance, Scr < 2.5 and K < 5
- Hydralazine/ISDN: better than nothing, consider in AA if unresponsive to ACE/ARB/BB
- LCZ696: Entresto: great outcomes II-IV
- Ongoing trials for HFpEF patients as well evaluating neurologic consequences
  - Heart failure decreases hospitalisations in pts with HR > 70, NR despite GDF
  - Be careful of fixed HR patients or restrictive and infiltrative, they may need HR to maintain CO
- IV iron: should be considered in HF patients who remain symptomatic despite OMM regardless if anemic or not, ongoing chronic IV iron may also be beneficial (benefits seen up to a year out)
- Ferritin < 100 μg/L or transferrin sat was < 20%

What’s new in Device therapy for Chronic HF?
- NECTAR-HF
- Chronic vagal stimulation
- CUPID
- Intracoronary infusion of SRCA 2a
- FIX-HF
- CCM: cardiac contractility modulation
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N=96  2:1 randomization
6 month follow up
Although no change in LV end syst diam
Significantly improved quality of life
Need larger trials

Multiple device based therapies to suppress the sympathetic nervous system or stimulate the vagal system

N=39 patients received IC adenovirus vector
AAV1 or AAV9
CUPID 2: press release 4/26/2015
was sadly negative - AAV1 vs AAV9

Cardiac Contractility Modulation
• Pacemaker like device
• Delivers energy to the myocardium during the absolute refractory period – no contraction with stimulation
• Causes changes that lead to increased intracellular calcium and therefore increased contractility

Duration 22ms
Amplitude ±7.5V

Electrocardiogram Output & CCM Application

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Clinical Trials Program for CCM

- **FIX-HF-4 study** - (168 patients) conducted in European Union - showed that 3 months of CCM treatment improved exercise tolerance and quality of life.
- **Fix HF-5** randomized 428 patients followed up for 1 year
  - Did NOT achieve primary end-point - analysis of anaerobic threshold measured on cardiopulmonary stress test
  - Showed significant improvements in the secondary end points:
    - Peak VO₂
    - Minnesota Living With Heart Failure Questionnaire score
  - First to show that patients with an LVEF between 35% and 45% benefited the most, whereas those with EF <25% derived inadequate benefit.
  - Circulation. 2018;138:2738-2740

Potential Role of CCM

- Heart Failure, NYHA III, Reduced EF, Symptomatic despite Optimal Medical Therapy
  - Wide QRS >130 msec
  - Narrow QRS CRT contraindicated

- CRT
- CCM

- Similar effects on functional status, quality of life, and exercise capacity

Take Away Points

- **Vagal nerve stimulation** did not improve markers of remodeling, but did improve symptoms, more to come
- Intracoronary infusion of AAV1/SERCA2a in patients with advanced heart failure, positive signals of cardiovascular events which persist for years.
  - No safety concerns were noted during the 3-year follow-up.
  - Larger scale CUPID 2 was negative:
    - Correct carrier AAV1 VS AAV9
    - Correct molecule to effect cell function? S100A1 (includes effect on cell energetics: MYK491003 [myosin activator])

- **Cardiac Contractility Modulation**
  - May have a beneficial effect in patient with EF 25-40% and continued symptoms despite GDMT and not CRT candidates.
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  • Evaluation for reversible causes
  • How to tell a patient is failing
• Chronic systolic heart failure
  • Current therapies
  • New Therapies
  • Medical
  • Device
  • Clinical trials
• Acute systolic heart failure
  • Current and new therapies
  • Heart transplant and mechanical circulatory support

How to know your patient may need advanced therapies:

**Early warning signs that an adult HF patient is starting to fail.**

• Severely reduced cardiac function
  • EF <30%
• Poor functional status
  • NYHA III/IV
  • Six minute walk: < 400 meters
  • Cardiopulmonary testing revealing poor cardiac reserve
  • VO2 <14 cc/kg/min
    • Cardiac limitation
    • Maximal medical therapy
  • Intolerance of NHB
  • Kittleson et al. JACC 2003;41:2029
  • Recurrent hospitalizations
  • Setoguchi et al. Am J Heart 2007
  • Need for inotropes
  • Kittleson et al. JACC 2003;41:2029
  • Hyponatremia
  • Renal insufficiency
  • Hillege HL et al. Circulation. 2000;102:203
    • Increasing diuretic need
    • Levy ESC HF 2003
  • Living in a smaller and smaller space
    • Circulation 1991;83:778-786
  • Electrical instability
    • Afib or ventricular arrhythmias

Severe Heart Failure
Recognizing the “Walking Wounded”

• Underperfused
  • Walk in, drive in, fly in
  • Obvious
    • Malignant arrhythmias
    • Low BP
  • Less Obvious (3Ts)
    • End organ underperfusion despite a normal BP
      • Told: lethargic; breathless at the end of a sentence
      • Touch: cool, pulses are low, lips/ears turn blue when they lay back for exam
      • Testing:
        • Lactate
        • Tki/LTs
        • Scr/BUN
Acute Decompensated heart failure vs SHOCK

- **ADHF:** congestion, possibly low output, quickly responsive to medical intervention
  - **Medical therapy**
- **SHOCK:** unstable hemodynamics, end organ underperfusion
  - **Device therapy**
    - Ischemic shock AMI
    - Hemodynamic shock
    - Arrhythmic shock

Goals of Therapy: *Chronic Versus Acute HF*

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<th>Long-Term Goals</th>
<th>Short-Term Goals</th>
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Prevent CHF Progression And Death

Relief of Symptoms
Stabilization of Organ Function

**RELAX-AHF and Pre RELAX-AHF Trials**

Concl. N=1395; Decreased 180 day mortality, markers of end organ damage (cr, transaminases) and markers of decongestion (BNP) were improved in the serelaxin group. Unfortunately

*RELAX-AHF2: approx 6800 pts; completed 1/26/17; ClinicalTrials.gov Identifier: NCT01870778: no benefit*
More About Congestion

PCWP after tailored therapy
Predicted outcomes

The CHAMPION Trial Abraham LANCET 2011

Protocol: If PAP pressures elevated:
1st: increase diuretics
second: increase vasodilators
Target Pressures:
sPAP: 15-35
dPAP: 8-20
mPAP: 10-25

LWS AJC 1990
PCWP after tailored therapy

Predicted outcomes

Congestion: what’s new with diuresis?

Murray AJM 2001
Ferreira EJM 2014

may be more effective, but use with caution: must watch Na, Potassium and magnesium!

Congestion: what’s new with diuresis?

The DOSE Trial
Felker NEJM 2011

Trend towards more weight loss in the high dose strategy and decreased DOE, it was at the cost of trend towards higher Scr (that did not last) out to 60 days.
Also, the low dose group did require an increase in dose.

Murray AJM 2001
Ferreira EJM 2014

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Mechanical Fluid Removal

Clinical Trial: Methods and Design

Cardiovascular Risk Study in Acute Decompensated Heart Failure: Rationale and Design of CONSENSUS-ADHF, for the Heart Failure United Research Network

Clinical trial design: randomized double-blind, placebo-controlled study

Primary endpoint: major adverse cardiovascular events

Secondary endpoints: hospitalization for heart failure, mortality, quality of life

UF lead to worse renal function and no decrease in hospitalizations

#POMA19

Inotropic Therapy in Patients With ADHF

- Routine use not indicated in short- or long-term setting (despite low EF)
- Rather, inotropes should only be used in patients with:
  - Cardiogenic shock ie: signs of end organ underperfusion
  - Decompensated patients refractory to diuretics
  - Short-term bridge to definitive treatment such as revascularization or cardiac transplantation
  - To optimize vasodilator therapy or add BB therapy


Inotropes

- Digoxin: improved QOL
- Dobutamine: beta agonist
- Milrinone: PDE inhibitor
- CLR325 trial: ongoing trial (apelin peptide)
- BMS study: BMS-986231 (nitroxyl)
- MYK491003: myosin activator

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Cardiogenic Shock definition

**Hemodynamic Definition**
- MAP 30 mmHg below baseline
- MAP ≤ 60
- CI < 1.8 without support
- CI < 2.0 with support
- LVEDp > 18 mmHg
- RVEDp > 10-15 mmHg

**Clinical signs**
- Depressed MS
- Decreased UO
- Liver insufficiency
- Elevated lactate

---

N=41 pts w AMICS encouraged HD monitoring and early MCS. 33% on inotropes. 15% out of hop arrest. 27% in hop cardiac arrest. 17% alive CPR while MCS deployment. Door to support time avg 83 minutes. 73% had inotropes decreased within 24 h of index procedure. 66% had MCS deployed before PCI.
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#### CARDIogenic Shock ALGORITHM

**Cardiogenic Shock Criteria**
- SBP < 90 mm Hg for 30 minutes
- Use of inotropes/vasopressors
- CI < 2.2 L/min/m²
- PWP > 18 mm Hg
- CPO < 0.6 W
- Lactate > 2 mmol/L

**Cardiogenic Shock Team**
- Cardiac Surgeon
- Cath Lab Attending
- MCS - Heart Failure specialist
- CCU Attending or CTSICU Attending

**Non-ACS**
- AMI shock
- Critically unstable
- Deep hypoxia + shock
- ECLS
- Electrical storm

**Non-AMI**
- Shock team activated
- Virtual shock rounds: “go” or “no go”

**Post Cardiotomy Shock**
- VA ECMO/Impella, bilateral Centrimag or Bipella
- VA ECMO/Impella or Centrimag LVAD

**Severe/profound Shock**
- Impella CP
- IABP

**Mild to moderate Shock**
- Protecuo - Impella RP
- LHF Impella 5.0 axill.
- Centrimag L
- Periph ECMO +/- Impella CP

**Ongoing Evaluation**
- Hemodynamics: CI, W, MAP, PAPi, CPO
- End organ perfusion: Lactate, Scr, LFTs

**Escalation of care if**
- CPO < 0.6
- CI < 2.2
- Rising: lactate, Scr, LFTs
- RHF = PAPi > 2, CVP/PCWP < 0.6
- ECMO +/- LV vent (central vs peripheral)

**Quality measures**
- Door to support time < 90 min
- Maintain CPO > 6 W
- Improve survival to discharge > 60%

**Temporary Devices**

**Impella 2.5, CP, 5.0**
- Increase Myocardial demand
- Tandem Heart ECMO

**Impella 5.0**
- Axillary access

**ECMO**

**Centrimag**
Post Support ICU care

- Determine ICU readiness
- Heparinize: 300 U/kg
- Continuous heparin 50-70 U/kg/h

- Start bedside monitor
- Anticoagulation with heparin

- Start inotropes
- Start pressors

- Wean pressors
- Wean inotropes

**Parameters Met**
- CI > 2.2
- MAP > 90 mmHg
- CPO > 0.6 W
- End organs normalized

**Parameters NOT met**
- CI  2.2
- MAP < 90 mmHg
- CPO < 0.6 W
- End organs worsening or not improving

Wean device

**Escalate care**

- Multidisciplinary ECMO Team

**V-A ECMO**

**Indications and Contraindications**

- Age > 65 years
- Severe respiratory failure
- Severe sepsis/septic shock
- Acute respiratory distress syndrome
- Acute lung injury
- Acute respiratory distress syndrome

**V-A ECMO Cannulation Options**

- Central cannulation

**Procedural Considerations**

- Insertion of central venous catheter
- Insertion of femoral arterial catheter

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Advanced Surgical Therapies: Heart Transplant or VAD Therapy

Heart Transplant vs LVAD/DT
How to Choose?

**Are they sick enough for Transplant/VAD?**
- Age over 65
- Concern for worsening comorbidities with immunosuppression
- DM
- Need to test compliance
- Recent smoking
- Recent non-compliance
- Need to test social support
- Malignancy < 5 years (treated) with a good prognosis

**Any other organs that limit life span?**
- Cancer
- Diabetes
- Lung disease
- Renal disease
- Liver disease
- Pulmonary HTN

**Are they healthy enough to undergo surgery?**
- Malnourished
- Too deconditioned
- Liver failure
- Do they have social support?

**Limitations are only cardiac**
- Intractable arrhythmias

**Inotropes**
- Poor cardiac reserve
- VO2 < 14

**Despite OMM**
- Limitations are only cardiac

**Are they sick enough for Transplant/VAD?**
- Listed but failing inotropes
- BTT: bridge to transplant
- DT: destination therapy
- BTD: bridge to decision
- BTT: bridge to transplant

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**Available VAD Devices**
- HeartMate II
- HeartMate 3
- HeartWare
- TAH
- MCS clinical Trials:
  - MOMENTUM
  - HM 3 vs HM II
  - STEM CELL Trial
  - VAD + endomyocardial stem cell injection
  - RESTAGE HF
  - VAD to recovery
- Future Devices:
  - MVAD
  - Circulite
Heart Failure Studies: understanding the failed heart

- **Human Heart Tissue Protocol** (Kenneth Margulies, MD)
  - To study heart tissue specimens in human heart failure. All patients listed for transplant or VAD are asked to participate.
  - As well as non-failing hearts that are not suitable for heart transplant
  - 3 types of hearts:
    - Failed (evaluated at time of OHT)
    - Failed but rested (after IABP support)
    - Non-failing heart
  - Dr. Margulies has assembled the largest biorepositories of human heart samples in the world
- **Samples**
  - Processed for study
  - With clinical data
  - Banked for future study
Heart Failure Studies

- Observations
  - Failed myocyte
    - Down regulation of B receptors
    - Deplete of SRCA 2a
- Recovery Plan
  - Promoting growth of new cells?
  - Improving function of existing cells?
  - VAD as a platform

What is the best method to recover a failing ventricle?

RESTAGE-HF Trial

- Early results
  - 5 sites, HM II
  - BTT or DT
  - Mean age 36 yo
  - HF <5 years, NICMP
  - Primary end point: recovery to explant and freedom from HF recurrence at one year (requirement for OHT/VAD)
  - Data of first 22 patients of 40 enrolled
    - 2 died post implant
    - Day #14 and #106
  - 5 of 20 reached predefined end point
    - 1 committed suicide
    - Support duration 222 d (14-445)
    - Mean age 45 yo (42-55)
    - 3 BTT
    - To date median 138 days post explant (14-383) of the remaining 4 patients

K Margulies, Biorepository, University of Pennsylvania
Recovery at Penn (CF era Eddie Rame, Wald, Atluri, Acker and Bermudez)

- Study Protocol
  - De novo
  - Stem cell therapy
  - LVAD platform
    - Clenbuterol
    - Stem cell Ph 1
    - Stem cell Ph 2
    - OMMP
    - CUPID Study
    - STOP-HF Study
    - EM, NM, MB, EC, KD, PP, AG, EB, LB, BS

- Planned
  - Short duration of HF*
  - Reversible insult
  - Surprise
  - Forced to Explant

*Not in clinical trial

Outcomes BTR vs BTT

Birks et al. J Thorac Cardiovasc Surg 2012;144:190-6

Conclusions

- Chronic heart failure
  - Ambulatory patients on medical therapy
    - BB therapy is important and dose matters
    - Aldosterone inhibitors are becoming a mainstay of therapy
    - Consider IV iron for symptomatic HF pts who are iron deficient
    - Ivabradine (if HR > 70 despite OMM) improved outcomes
    - FDA approved, to decrease hospitalisations
  - LCZ696: angiotensin neprilysin inhibitor: ambulatory and ADHF
  - Targeting congestion is important to patient outcomes
    - Cardiomeps PA monitoring
    - Target recovery: besides aggressive medical therapy,
      - cell therapy, gene therapy, mechanical support
    - There are new devices on the horizon that may make an impact
      - Cardiac Contractility Modulation

Conclusions (cont’d)

- Acute decompensated heart failure
  - IV diuresis bolus = continuous, high dose better
  - Seralaxin may have a benefit REUS-AHF 2 is underway

- Advanced heart failure
  - End organ under perfusion or severe symptoms despite maximal therapy
  - Acutely ill, refractory to medical therapy
    - Temporary devices
      - IABP
      - Impella 2.5, CF 5.0
      - Tandem heart, RP
      - ECMO
    - Permanently Platforms: better outcome with earlier tx
      - Heart transplant
      - Durable VADs (Mechanical Circulatory Support)- think of RECOVERY
        - HM I/II
        - Heartware
      - with exciting new, smaller, fully implantable devices on the horizon

Thank you!!!