Phosphodiesterase Type 5 Inhibition with Tadalafil CHanges Outcomes in Heart Failure (PITCH-HF)

CCC Principal Investigator: Marc J. Semigran, MD
Massachusetts General Hospital, New England Research Institutes, NHLBI

Supported by the National Heart Lung and Blood Institute (NHLBI)

Background
Pulmonary hypertension (PH) and right ventricular dysfunction is important in prognosis and functional capacity in HF due to left ventricular systolic dysfunction (LVSD). Chronic tadalafil therapy will have a beneficial effect on clinical outcomes in HF patients with LVSD and secondary PH.

Hypothesis
Chronic tadalafil therapy will have a beneficial effect on clinical outcomes in HF patients with LVSD and secondary PH.

Primary Endpoint
Time to either cardiovascular (CV) mortality or HF hospitalization

Secondary Endpoints
Time to CV mortality
Time to HF hospitalization
Time to all-cause mortality
Time to all-cause mortality or CV hospitalization
Frequency of CV hospitalizations
Frequency of HF hospitalizations
Change in 6 MWD from baseline to 3 and 18 months
Change in MLHFQ from baseline to 3 and 18 months

Major Inclusion Criteria
- Age 21 or older
- NYHA class II-IV with LVSD (LVEF < 0.40)
- At high risk of future clinical instability or decompensation
- BNP ≥ 300 pg/mL or NTproBNP ≥ 1800 pg/mL within 3 months
- HF hospitalization within last 12 months
- Secondary PH within last 6 months
- Echocardiography: RVSP ≥ 40 mmHg or mean PAP ≥ 25 mmHg at rest
- Catheterization: mean PAP ≥ 25 mmHg at rest or mean PAP ≥ 35 mmHg with exercise
- Treatment according to current AHA/ACC guidelines
- Stable medical therapy for 30 days prior to randomization
- No contraindications to PDE5 inhibitor therapy (e.g. nitrates)

Trial Design
Screening/Enrollment
- NYHA Class II-IV HF
- LVEF 40%, Secondary PH
- Optimal HF pharmacotherapy
- Informed Consent

Baseline
- H&P, MLHFQ, check, ICD check 6-WD, Blood collection, Meds

Randomization
- Placebo n=1051
- Tadalafil n=1051

Treatment
- Dose: 20 mg qD, uptitrate to 40 mg qD at 1 week if tolerated

POST-Randomization Follow-Up Clinical Assessments
- 1 wk, 1mo, 3 mo, 6 mo, Q6 mo followup (max 36 mo)

Ancillary Studies
- PITCH-ER: Aims to evaluate the effects of tadalafil vs. placebo on measures of chronic and acute renal injury and to explore the mechanisms underlying these anticipated effects.
- PITCH-RIGHT: Aims to determine if treatment with tadalafil improves RV-PV reserve through the use of traditional and novel measurements.

References
1. Ghio SJ, JACC 2001
3. Guazzi M, Circ Heart Fail 2011;4:8-17

Acute administration of sildenafil improves peak VO2 in NYHA II-III HF patients with secondary pulmonary HTN (mean PA > 25 mmHg) by 15%.
Chronic PDE5 inhibition (sildenafil) improves exercise capacity and reverses LV remodeling after 12 months.

WE ARE STILL RECRUITING SITES!

Complete a site survey!
Site activation and certification: NOW
First patient in: Nov 18th, 2013

Supported by the National Heart Lung and Blood Institute (NHLBI)