Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT)

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Introduction In the absence of a proven therapy to improve the prognosis of patients with heart failure and preserved LV ejection fraction (HFpEF) treatment remains empirical. Mineralocorticoid receptor antagonists have been shown to reduce the risk of death and other major cardiovascular events in patients with reduced EF heart failure and following myocardial infarction.

Hypothesis Treatment Of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) is a NHLBI contract, international randomized placebo controlled trial evaluating the effectiveness and safety of spironolactone (15mg titrated to 45mg) compared to placebo in patients with HFpEF, using time to first event cardiovascular mortality, aborted cardiac arrest, or heart failure hospitalization as the primary endpoint.

Methods Inclusion criteria were informed consent, age ≥ 50 years, symptomatic HF, LVEF ≥ 45%, HF hospitalization (within 12 months, Stratum I) or an elevated BNP or NT proBNP (≥100 or 360 pg/ml, Stratum II). Recent stroke, coronary event, uncontrolled hypertension, eGFR < 30, and hyperkalemia (≥5.0 mmol/L) were some of the major exclusions. Subjects were randomized within each stratum and followed for 3.4 years on average. Safety assessments, nonfatal cardiovascular events, the development of atrial fibrillation, diabetes mellitus and quality of life were key secondary endpoints.

Results There were 3445 participants, 2480 and 965 in stratum I and II, respectively with country totals: USA 1151, Russia 1066, Republic of Georgia 612, Canada 326, Brazil 167 and Argentina 123. TOPCAT subjects were 68.6 ± 9.6 years old, 52% female, 63% NYHA II, 33% NYHA III and had a mean LVEF 57±7%. Baseline comorbidities included hypertension 91%; coronary artery disease 59%; chronic kidney disease 38%; atrial fibrillation 35%; and diabetes mellitus 32%. Key baseline measures were: Blood Pressure 129±14/76±11 mmHg; Heart Rate 69±10/min; BMI 32.1±7.3 kg/m2; eGFR 67.7±20.1 mL/min /1.73m2; Median Urine Microalbumin 20.0 IQR (7.0, 88.4) mg/g creatinine.

Conclusion The Data Safety Monitoring Committee allowed the trial to complete follow-up uninterrupted. This AHA submission represents the first public presentation of the TOPCAT trial results. NCT00094302

M.A. Pfeffer: Research Grant; Significant; Amgen, Celladon, Novartis, Sanofi-Aventis. Consultant/Advisory Board; Modest; Aastrom, Amgen, Bristol-Myers Squibb, Cerenis, Concert, Genzyme, Hamilton Health Sciences, Keryx, Medtronic, Merck, Novartis, Roche, Servier, University of Oxford and Xoma. Consultant/Advisory Board; Significant; Teva. Other; Modest; Brigham & Women’s Hosp has patents for use of inhibitors of the RAS in selected survivors of MI. Dr. Pfeffer’s share of the licensing agreement with Novartis is irrevocably transferred to charity. S. McKinlay: None. B. Pitt (for the TOPCAT Investigators): Consultant/Advisory Board; Modest; Pfizer, Bayer, Merck, Novartis, Takeda, Bristol-Myers Squibb, Astra Zeneca, BG-Medicine and Relypsa. Other; Modest; Equity Interests in BG-Medicine and Relypsa.