A Randomized Trial of Liraglutide for High-Risk Heart Failure Patients with Reduced Ejection Fraction

Kenneth B Margulies, Univ of Pennsylvania, Philadelphia, PA; Kevin J Anstrom, Duke Univ, Philadelphia, PA; Margaret M Redfield, Mayo Clinic, Rochester, MN; Michael M Givertz, Brigham and Women's Hosp, Boston, MA; Guilherme H Oliveira, UH Case Medical Ctr, Cleveland, OH; Robert Cole, Emory Univ, Atlanta, GA; Doug Mann, Washington Univ in St. Louis, St. Louis, MO; David J Whellan, Thomas Jefferson Univ, Philadelphia, PA; Michael S Kiernan, Tufts Univ, Boston, MA; G. Michael Felker, Steven E McNulty, Duke Univ, Durham, NC; Monica R Shah, Natl Heart Lung and Blood Inst, Bethesda, MD; Adrian F Hernandez, Duke Univ, Durham, NC; Eugene Braunwald, Brigham and Women's Hosp, Boston, MA; Thomas P Cappola, Univ of Pennsylvania, Philadelphia, PA

**Background:** The heart consumes more energy per gram than any other organ, and myocardial metabolic demands are further increased in the failing heart. As heart failure (HF) progresses, the myocardium develops defects in substrate utilization including reduced fatty acid utilization and insulin resistance that impair glucose uptake. Synthetic GLP-1 agonists improve insulin sensitivity and represent promising metabolic modulators for patients with HF.

**Methods:** The Functional Impact of GLP-1 for Heart Failure Treatment (FIGHT) study is a randomized, double-blinded, placebo-controlled clinical trial in high-risk HF patients with reduced ejection fraction (LVEF ≤ 40%) and recent hospitalization. 300 subjects were randomized to treatment with either the GLP-1 agonist liraglutide or placebo delivered by daily SQ injection. FIGHT included patients with and without type-2 diabetes, and a randomized block design to assure equal allocation of diabetics and non-diabetics to the two treatment arms. The primary end point of FIGHT is a global rank endpoint in which all participants, regardless of treatment assignment, are ranked across three hierarchical groups: 1) time to death, 2) time to HF hospitalization, and 3) time-averaged proportional change in NT-proBNP (from baseline to 180 days). The principal secondary end points include change in cardiac structure and function (by echocardiography) from baseline to 180 days. Additional endpoints include functional status based on the six-minute walk distances at 30, 90, and 180 days, changes in symptoms, based on the KCCQ, from baseline to 180 days, and individual components of the primary endpoint at 30, 90 and 180 days after randomization.

**Results:** Enrollment in FIGHT was completed in March 2015 and follow up and database finalization will be completed in September. Baseline characteristics of the 300 patients include (median (25th, 75th) or %): Age 61 years (51, 68); Female 21%; Black 38%; Ischemic heart disease 82%, Hypertension 79%; Diabetes 60%; NYHA II/III 29%/65%, and LVEF 23% (17, 27).

**Conclusion:** FIGHT is the first multicenter trial of a GLP-1 receptor agonist in the treatment of high-risk HF with reduced ejection fraction and will determine if this intervention improves clinical status at 180 days.

**Disclosure:**

**K.B. Margulies:** Consultant/Advisory Board; Modest; Merck, Sharp and Dohme; Pfizer, Inc. **K.J. Anstrom:** Research Grant; Modest; AstraZeneca. Consultant/Advisory Board; Modest; Pfizer, Abbot Vascular, AstraZeneca. **M.M. Redfield:** Honoraria; Modest; Heart Failure Society of America. Consultant/Advisory Board; Modest; Novartis (unpaid). Other; Modest; Anexion (Royalties). **M.M. Givertz:** Research Grant; Modest; Bristol Myers Squibb, Merck, Portola. Research Grant; Significant; AstraZeneca, Glaxo Smith Kline. Consultant/Advisory Board; Modest; Amgen, AstraZeneca, Bayer, Bristol-Myers Squibb, Gilead, Glaxo Smith Kline, Janssen, Merck, Pluristem Therapeutics, Inc., Sensible. Consultant/Advisory Board; Significant; Novartis. **G.H. Oliveira:** Research Grant; Significant; Frankino-Dodero Foundation. Speakers
Bureau; Modest; Amgen, Novartis. Consultant/Advisory Board; Modest; Abiomed. R. Cole: None. D. Mann: None. D.J. Whellan: Research Grant; Significant; ResMed, Poszen. M.S. Kiernan: None. G. Felker: Research Grant; Significant; Roche Diagnostics, Novartis, Amgen, Otsuka, Singulex. Consultant/Advisory Board; Modest; Trevena, Merck, Celladon. Consultant/Advisory Board; Significant; Novartis, Amgen. S.E. McNulty: None. M.R. Shah: None. A.F. Hernandez: Consultant/Advisory Board; Modest; Novartis, Janssen, Bristol-Myers Squibb. E. Braunwald: Research Grant; Significant; AstraZeneca. Consultant/Advisory Board; Modest; Genzyme, Amorcyte, Medicines Co., CardioRentis, Sanofi-Aventis. Other; Modest; Eli Lilly (Lectures), Daichi Sankyo (Lectures), Menarini International (Lectures), Medscape (Lectures), Bayer (Lectures). T.P. Cappola: Consultant/Advisory Board; Modest; Teva Pharmaceuticals, Novartis.