Dapagliflozin Alone or Combined with Ramipril Improves Hyperglycemia, Hypertension, and Prevents Kidney Complications and GFR Decline in the Nephrectomized SDT Fatty Rat Model of Diabetic Nephropathy.

François Briand1, Masami Shinohara2, Emmanuel Brousseau1, Takeshi Ohta3, Yasushi Kageyama2, Thierry Sulpice1

1Physiogenex, Labège, France; 2CLEA Japan Inc., Meguro-ku, Tokyo, Japan; 3Japan Tobacco Inc., Osaka, Japan

RESULTS

1. A 10-week dapagliflozin treatment does not alter GFR but significantly improves kidney complications in Unx SDT fatty rat under 0.3% salt.

2. Dapagliflozin in combination with ramipril for 10 weeks results in similar glycemic control but further reduces hypertension compared to dapagliflozin alone.

3. Dapagliflozin in combination with ramipril for 10 weeks better prevents severe GFR decline than dapagliflozin alone.

METHODS

Male, 6-week old SDT fatty rats underwent unilateral nephrectomy. After a 1-week recovery, rats had free access to Purina 5008 chow diet and drinking water supplemented with 0.3% salt for 10 weeks. Rats were treated without (CTRL) or either with DAPA 1mg/kg/day alone or with DAPA + RAMI both at 1mg/kg/day, in the diet, upon diet start (10-week treatment; n=7 per group).

Glomerular Filtration Rate (GFR) was assessed using FITC-insulin i.v. injection at different timepoints: before and 1-week after unilateral nephrectomy (treatment start), then at 5 and 10 weeks of treatment.

At the end of the treatment period, blood pressure (tail-cuff plethysmography) and biochemical parameters from blood, plasma and urine samples, were measured.

Kidney was collected for histology (Periodic Acid Schiff (PAS), Coll III and ED1 immunostaining prior to a blinded histopathology scoring.

Data are presented as mean ±SEM. Statistical analysis was performed using either an unpaired, 2 tailed Student t-test, Mann-Whitney test or a 1-way ANOVA + Bonferroni post-test. A p<0.05 was considered significant.

DISCLOSURES

FB, EB and TS are employees of Physiogenex. MS and YK are employees of CLEA Japan Inc. TO is an employee of Japan Tobacco Inc.