Effects of liraglutide in the SDT fatty rat – a type 2 diabetic cardio-renal model
Study design

SDT fatty rat, male 5-week old, n=40

10-week acclimation

15-w of age

randomization:
- Glomerular Filtration Rate (Medibeacon)
- blood glucose
- body weight

Control or liraglutide s.c. QD 0.4mg/kg/day

4-week treatment:
- Glomerular Filtration Rate (Medibeacon)
- blood glucose & urine parameters

20-w of age/5-week treatment:
unilateral nephrectomy

0.3% salt supplemented drinking water for 5 weeks

hyperfiltration phase

GFR decline phase

25-w of age

histology analysis

10-week treatment:
- Glomerular Filtration Rate (Medibeacon)
- blood glucose & urine parameters

25-w of age

6-week treatment:
blood glucose

15-w of age

10-week treatment:
- Glomerular Filtration Rate (Medibeacon)
- blood glucose & urine parameters

- echocardiography (systolic/diastolic function)
- systolic/diastolic blood pressure/heart rate

15-w of age

6-week treatment:
- Glomerular Filtration Rate (Medibeacon)
- blood glucose & urine parameters
Diabetic nephropathy
Body weight follow-up

unilateral nephrectomy at 5 weeks

- Vehicle
- Liraglutide

Body weight (g)

weeks of treatment
Body weight gain/loss follow-up

- **vehicle**
- **liraglutide**

*unilateral nephrectomy at 5 weeks*

Body weight gain (g)

weeks of treatment

- **vehicle**
- **liraglutide**
Fed blood glucose follow-up

**Fed Blood Glucose**

- **Blood glucose (mg/dL)**
  - Y-axis range: 0 to 800

**Weeks of Treatment**

- X-axis range: 0 to 10

**Vehicle**
- Open circles

**Liraglutide**
- Green circles

**Unilateral Nephrectomy at 5 weeks**

- Arrow indicating unilateral nephrectomy at 5 weeks

Significance levels:
- ***: P < 0.001
- *: P < 0.05

*Physiogenex The Metabolic Disease Experts*
Urine albumin/creatinine ratio follow-up

Unilateral nephrectomy at 5 weeks

- **Vehicle**
- **Liraglutide**

Graph showing urine albumin/creatinine ratio (µg/mg) over weeks of treatment.
Glomerular filtration rate follow-up (FITC-sinistrin & Medibeacon transdermal monitor)

unilateral nephrectomy at 5 weeks

- **vehicle**
- **liraglutide**

weeks of treatment

glomerular filtration rate (mL/min/kg)
Kidney histopathology (PAS staining - glomerulosclerosis)

vehicle

LIRA
Kidney histopathology (collagen III staining - fibrosis)

Vehicle

LIRA
Kidney histopathology

- % ED1 staining
- Macrophages / cm²
- % collagen III staining
In SDT fatty rats and in the present experimental conditions:

- Liraglutide reduces hyperglycemia.
- Liraglutide reduces hyperfiltration, while it prevents the GFR decline after unilateral nephrectomy.
- Liraglutide reduces kidney inflammation and fibrosis.

Given the benefits of liraglutide, further cardiovascular characterization was then performed.
blood/intraventricular pressure and echocardiography measurements at 10 weeks of treatment
Blood pressure and intraventricular pressure

Control = chow fed Sprague Dawley rats (baseline/control values)
Left ventricular volume and wall thickness

LV end-diastolic volume (μL)

LV end-systolic volume (μL)

Anterior wall thickness in diastole (mm)

Anterior wall thickness in systole (mm)
Heart and left ventricle weight
Diastolic and systolic function

![Diastolic and systolic function graphs](image-url)
In SDT fatty rats and in the present experimental conditions:

- Liraglutide reduced both arterial and left ventricle end-systolic pressures and tended to reduce end-diastolic pressure.

- Liraglutide significantly reduced both left ventricle enlargement and wall thickness.

- SDT fatty rats showed diastolic dysfunction with preserved systolic function (preserved ejection fraction and fractional shortening). Liraglutide normalized diastolic function.