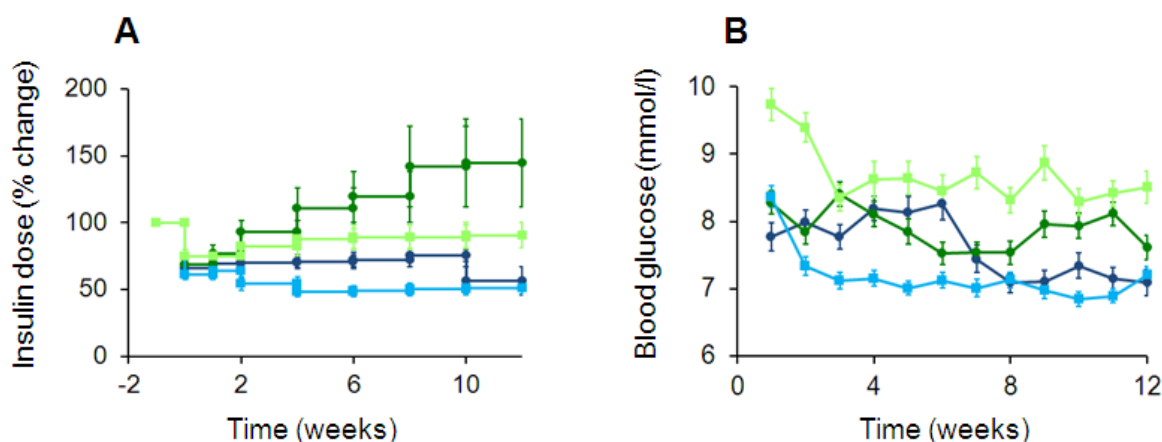


SUPPLEMENTARY DATA

Supplementary Figure 1. Change from baseline insulin dose and blood glucose measurements. Percent change from baseline insulin dose during the trial period in participants treated with insulin at baseline (A) and blood glucose measurements (B) in patients with type 2 diabetes and dialysis-dependent end-stage renal disease treated with liraglutide (dark blue curves) and placebo (dark green curves) and in control persons with type 2 diabetes and normal kidney function treated with liraglutide (light blue curves) and placebo (light green curves). Data are means \pm standard error based on data from the per protocol population. Blood glucose was reduced from baseline to Week 12 in all groups ($P < 0.01$). In parallel, doses of basal insulin were significantly reduced in both liraglutide-treated groups during the study period ($P < 0.04$).



SUPPLEMENTARY DATA

Supplementary Table 1. Clinical and biochemical changes during intervention

	ESRD				Control			
	Placebo N=10	Liraglutide N=10	Diff (95% CI)	P	Placebo N=10	Liraglutide N=10	Diff (95% CI)	P
Clinical								
Weight (kg, $\Delta 0$ -12 weeks)	-0.2 \pm 1.3	-2.4 \pm 0.8	-2.1 (-5.6 to 1.4)	0.22	-0.3 \pm 0.5	-2.9 \pm 1.0	-2.6 (-4.8 to -0.3)	0.03
Pulse (min ⁻¹ , $\Delta 0$ -12 weeks)	-10.2 \pm 2.7	6.9 \pm 2.4	16.4 (8.5 to 24.4)	<0.01	1.1 \pm 3.9	5.5 \pm 2.3	4.4 (-5.2 to 14.0)	0.35
Sys BP (mmHg, $\Delta 0$ -12 weeks)	-3.6 \pm 6.1	-3.6 \pm 10.4	0.1 (-24.7 to 24.8)	1.00	-7.4 \pm 5.1	-3.1 \pm 3.9	4.3 (-9.1 to 17.7)	0.51
Dia BP (mmHg, $\Delta 0$ -12 weeks)	0.8 \pm 3.7	4.8 \pm 3.0	4.0 (-6.2 to 14.1)	0.42	-3.7 \pm 3.2	0.2 \pm 2.3	3.9 (-4.3 to 12.1)	0.33
Blood samples								
Haemoglobin A1c (% (mmol/mol), $\Delta 0$ -12 weeks)	-0.4 \pm 0.3 (-4 \pm 3)	-0.5 \pm 0.3 (-6 \pm 3)	-0.1 (-1.0 to 0.7) (-1 (-11 to 8))	0.71	-0.3 \pm 0.3 (-3 \pm 3)	-1.3 \pm 0.4 (-14 \pm 4)	-1.0 (-2.0 to -0.1) (-11 (-22 to -1))	0.03
Creatinine (μ mol/l, $\Delta 0$ -12 weeks)	0 \pm 1	-1 \pm 2	-1 (-11 to 8)	0.78	1 \pm 1	0 \pm 1	-2 (-11 to 7)	0.72
Albumin (g/l, $\Delta 0$ -12 weeks)	0 \pm 1	-1 \pm 2	-1 (-5 to 3)	0.54	1 \pm 1	0 \pm 1	1 (-2 to 2)	0.93
Alanine amino-transferase (U/l, $\Delta 0$ -12 weeks)	-2 \pm 2	-3 \pm 5	-1 (-11 to 8)	0.78	-3 \pm 3	-4 \pm 3	-2 (-11 to 7)	0.72
Calcitonin (pmol/l, $\Delta 0$ -12 weeks)	-0.3 \pm 0.2	0.1 \pm 0.8	0.4 (-1.5 to 2.3)	0.66	0.1 \pm 0.1	0.1 \pm 0.1	0.1 (-0.3 to 0.4)	0.67
ProBNP (pmol/l, $\Delta 0$ -12 weeks)	176 \pm 135	-184 \pm 62	-360 (-675 to -45)	0.03	3 \pm 5	-1 \pm 1	-4 (-16 to 7)	0.45
Total cholesterol (mmol/l, $\Delta 0$ -12 weeks)	-0.5 \pm 0.5	-0.3 \pm 0.2	0.2 (-0.9 to 1.3)	0.68	0.2 \pm 0.2	-0.5 \pm 0.1	-0.7 (-1.1 to -0.2)	0.01
LDL cholesterol (mmol/l, $\Delta 0$ -12 weeks)	-0.4 \pm 0.4	-0.3 \pm 0.2	0.1 (-0.9 to 1.0)	0.9	0.1 \pm 0.2	-0.4 \pm 0.1	-0.5 (-0.9 to -0.1)	0.03
HDL cholesterol (mmol/l, $\Delta 0$ -12 weeks)	-0.1 \pm 0.1	-0.2 \pm 0.1	-0.1 (-0.4 to 0.2)	0.47	0.0 \pm 0.1	-0.1 \pm 0.1	-0.2 (-0.3 to 0.0)	0.05
Triglyceride (mmol/l, $\Delta 0$ -12 weeks)	-0.11 \pm 0.33	0.32 \pm 0.16	0.43 (-0.37 to 1.22)	0.27	0.08 \pm 0.16	0.00 \pm 0.26	-0.08 (-0.72 to 0.57)	0.81

Changes in clinical and biochemical parameters during intervention ($\Delta 0$ -12 weeks) and comparison between groups. Data are presented as mean \pm standard error and mean difference between groups with 95% confidence interval in brackets. For those biochemical parameters reported with a lower detection limit an exact result was estimated as half the lower detection limit (calcitonin: 0.3 pmol/l; proBNP: 2.95 pmol/l). Dia BP, diastolic blood pressure; ESRD, end-stage renal disease; HDL, high density lipoprotein; LDL, low density lipoprotein; proBNP, prohormone brain natriuretic peptide; Sys BP, systolic blood pressure.

SUPPLEMENTARY DATA

Supplementary Table 2. Adverse events

	ESRD + liraglutide	ESRD + placebo	Control + liraglutide	Control + placebo	<i>P</i>
N	14	10	11	12	
Gastrointestinal					
Nausea (days)	[200] 4 (86) *	[52] 1 (35)	[59] 0 (22)	[7] 0 (7)	0.06
Vomiting (days)	[71] 1 (43) *	[2] 0 (2)	[8] 0 (4)	[0] 0 (0)	0.02
Diarrhoea (days)	[13] 0 (5)	[14] 0 (9)	[63] 0 (37) *	[4] 0 (3)	0.01
Dyspepsia (days)	[176] 3 (51)	[1] 0 (1)	[155] 5 (61)	[3] 0 (3)	0.136
Reduced appetite (days)	[216] 0 (83)	[9] 0 (9)	[184] 28 (83)	[88] 0 (88)	0.10
Flatulence (days)	[0] 0 (0)	[77] 0 (70)	[90] 2 (53)	[21] 0 (13)	0.20
Abdominal discomfort (days)	[14] 0 (14)	[40] 0 (18)	[128] 0 (59) *	[6] 0 (4)	< 0.01
Constipation (days)	[6] 0 (4)	[49] 0 (21)	[18] 0 (11)	[24] 0 (24)	0.12
Miscellaneous					
Headache (days)	[1] 0 (1)	[50] 0 (28)	[44] 2 (19)	[24] 0 (15)	0.29
Dizziness (days)	[9] 0 (9)	[32] 0 (19)	[8] 0 (8)	[17] 0 (9)	0.17
Fatigue (days)	[98] 0 (84)	[135] 6 (42)	[148] 7 (48)	[25] 0 (14)	0.20
Fever (days)	[1] 0 (1)	[2] 0 (2)	[20] 0 (12) *	[5] 0 (5)	0.01
Nasopharyngitis/bronchitis (episodes)	[3] 0 (1)	[6] 1 (1)	[6] 0 (2)	[2] 0 (1)	0.16
Minor hypoglycaemia (episodes)	[9] 1 (3)	[3] 0 (1)	[0] 0 (0)	[10] 0 (5)	0.34
Injection site reactions (episodes)	[2] 0 (1)	[4] 0 (1)	[7] 1 (2)	[5] 0 (2)	0.27

Adverse events in the intention to treat population. Data are sum in square brackets, median and range in normal brackets. Asterisks (*) indicate $P < 0.05$.

SUPPLEMENTARY DATA

Supplementary Table 3. Severe adverse events, drop outs and exclusions

	ESRD N=24	Liraglutide group (Y/N)	Control N=23	Liraglutide group (Y/N)
Severe adverse event (cause, N)	<ul style="list-style-type: none"> - Chest pain and infection (N=1) - Clotted AV fistula (N=2) - Catheter infection (N=1) - GI bleeding (N=1) - Lumbar spinal stenosis (N=1) - Appendicitis acuta (N=1) 	<ul style="list-style-type: none"> Y Y, Y Y N Y Y 	<ul style="list-style-type: none"> - Knee arthroscopy (N=1) 	<ul style="list-style-type: none"> Y
Dropout/ exclusion (cause, N)	<ul style="list-style-type: none"> - Low compliance (N=1) - Admittance (N=2) - Change in dialysis location (N=1) - Holiday (N=1; included in the PP population) 	<ul style="list-style-type: none"> Y Y, Y Y Y 	<ul style="list-style-type: none"> - Time consumption (N=1) - Dizziness (N=1) - Exanthema (N=1) 	<ul style="list-style-type: none"> N N Y

Based on data from the intention to treat population. All severe adverse events led to admission. AV, arterio-venous; GI, gastrointestinal; PP, per protocol