SUPPLEMENTARY DATA

Description and summary of placement procedure for ITCA 650

ITCA 650 utilizes a novel drug delivery technology to provide continuous and controlled subcutaneous delivery of exenatide at a precise and predetermined rate for the nominal dosing period of each pump. ITCA 650 releases drug at a predetermined rate based on osmosis. Extracellular fluid enters through the semi-permeable membrane directly into the osmotic engine (salt gradient). The resulting pressure pushes the piston at a slow and consistent rate of travel and forces the drug formulation to be released through the orifice of the diffusion moderator. In this study, ITCA 650 mini-pumps delivering exenatide for 3 and 6 months were evaluated. Initiating treatment with ITCA 650 requires the subdermal placement of a matchstick-size osmotic mini-pump during a short office procedure that can be performed by a physician, physician's assistant or other licensed practitioner. The figure provides an illustration of ITCA 650. ITCA 650 consists of a cylindrical titanium alloy reservoir with external dimensions of 4 mm in diameter by 44 mm in length. The reservoir is capped at one end by a controlled-rate, semi-permeable membrane and capped at the other end by a diffusion moderator through which drug formulation is released from the drug reservoir. The drug formulation, piston and osmotic engine are contained inside the cylinder.

Supplementary Figure 1. ITCA 650 osmotic mini-pump

SUPPLEMENTARY DATA

Schematic of ITCA 650

Rescue Criteria

Criteria for rescue therapy were, between Day 14 and Week 13, two or more fasting self-monitored blood glucose (SMBG) values >240 mg/dL during any 7 day period and confirmed by a fasting plasma glucose (FPG) determination at the study site within 7 days; following Week 13, two or more fasting SMBG values >200 mg/dL during any 7 day period and confirmed by a FPG determination at the study site within 7 days; an HbA1c elevation of at least 1.5% from Day 0 or an HbA1c >8.5% at Week 26 and onwards. Rescue therapy consisted of insulin glargine at 0.2 units/kg at bedtime and increased by 2 units every 3 days as needed until the FPG was adequately controlled. Alternatively, at the discretion of the Investigator, additional antidiabetic medication was prescribed, and/or modifications made to background therapy. Dipeptidyl peptidase-4 (DPP-4) inhibitors, incretin mimetics and sodium-glucose co-transporter 2 (SGLT2) inhibitors were not allowed for rescue therapy.

Hypoglycemia

If, following Day 0, the patient had an SMBG value <60 mg/dL with or without symptoms (e.g., diaphoresis, weakness, tachycardia, change in mental status) the Investigator inquired about the presence or absence of confounding factors that could explain the hypoglycemia (e.g., increased physical activity, intercurrent illness, skipped meal). In the presence of such confounding factors, the Investigator advised the patient on how to avoid similar episodes in the future. In the absence of confounding factors, the dose of background SU therapy was decreased at the Investigator's discretion.

Additional Laboratory Tests

A lipid profile (total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglyceride) and serum levels for thyroid stimulating hormone, high-sensitivity C-reactive protein (hsCRP), adiponectin, and ApoB-100 were obtained at screening or baseline and at Week 39. Serum calcitonin was measured at screening, baseline, and weeks 13, 26, and 39. Serum amylase and lipase were measured at screening, baseline, weeks 1, 6, 13, 26, and 39, and at follow up. Insulin resistance was assessed by the homeostasis model index-insulin resistance (HOMA-IR), and beta cell function was assessed by the homeostasis model index-beta (HOMA-β). Glomerular filtration rate (GFR) was calculated using the isotope dilution mass spectrometry-traceable Modification of Diet in Renal Disease Study equation.

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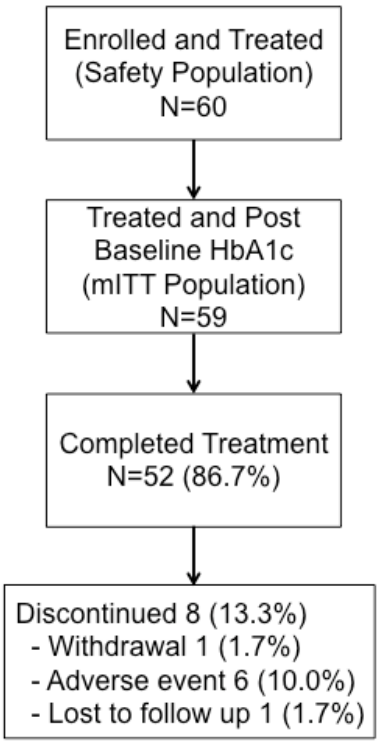
Supplementary Figure 2. Study Flow Chart.



Supplementary Table 1. Mean change from baseline to Week 39 (mITT Population, LOCF analysis).

Parameter	Mean (SD) Change
Systolic blood pressure (mm Hg)	0.8 ± 12.4 p=0.638
Diastolic blood pressure (mm Hg)	1.5 ± 7.0 p=0.097
Total cholesterol (mmol/L)	-0.19 ± 1.30 p=0.375
LDL-cholesterol (mmol/L)	-0.12 ± 1.16 p=0.566
HDL-cholesterol (mmol/L)	0.06 ± 0.19 p=0.065
Triglyceride (mmol/L)	-0.37 ± 1.04 p=0.035[a]
Apolipoprotein B (g/L)	-0.12 ± 0.30 p=0.023[a]

[a] p-value is one same t-test for Week 39 vs. baseline.

SUPPLEMENTARY DATA

Supplementary Table 2. Mean change from baseline to Week 39 – Safety Population.

Parameter	Mean (SD) Change
Amylase (U/L)	14.0 ± 17.5 p<0.001[a]
Lipase (U/L)	16.7 ± 31.8 p<0.001[a]
Calcitonin (pg/mL)	0.2 ± 1.5
Heart rate (bpm)	4.5 ± 9.5

[a] p-value is Wilcoxon signed rank test for within patient variability over time