1107-P

Efficacy and Tolerability of 39 Weeks of ITCA 650 (Continuous Subcutaneous Exenatide) in Poorly Controlled T2DM With High Baseline A1C (>10%)

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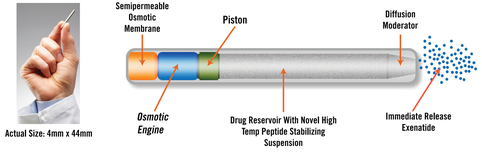
BACKGROUND

- A large segment of treated patients with Type 2 diabetes mellitus (T2DM) remain poorly controlled due to:
  - The progressive nature of the disease
  - Limitations of current regimens; clinical inertia
  - Poor therapeutic compliance and adherence over time
- The benefits of GLP-1 therapy as a class include lowering HbA1c, weight loss, low hypoglycemic risk
- The potential risks include poor adherence with injectables and their relegation to later in treatment and the cost of poor adherence overall
- ITCA 650 osmotic mini-pump is an injection-free GLP-1 receptor agonist, currently in Phase 3 development, that can deliver exenatide subcutaneously for up to 12 months (**Figure 1**)
- Osmotic mini-pump – size of small matchstick
  - Continuous zero order delivery of drugs
  - Novel suspension stabilizes peptides at high body temperatures
  - Sub-dermal placement once/twice yearly in a short, in-office, sterile procedure
  - Procedures are done by Specialists, PCPs, and Nurse/PAs
  - Approved reimbursement codes for similar procedures in the US
- In Phase 2, ITCA 650 treatment resulted in significant HbA1c reductions over 48 weeks in metformin treated patients with baseline HbA1c of 8%
  - Sustained HbA1c reduction of 1.4%
  - 3.0-4.0 kg weight loss
  - Well tolerated
    - Observed low discontinuation rates with doses taken into phase 3

Figure 1. Intarcia Delivery Technology



OBJECTIVES

- FREEDOM-1 was a double-blind, randomized, multicenter, placebo-controlled study of ITCA 650 in patients with HbA1c ≥7.5% to ≤10.0%
- Patients who met all inclusion criteria for FREEDOM-1 but who had a HbA1c >10% but ≤12% were enrolled in FREEDOM-1HBL

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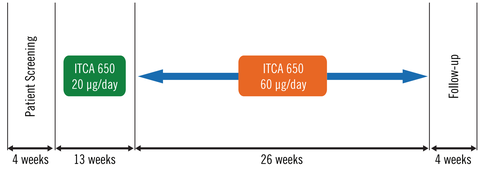
- FREEDOM-1HBL was an open-label study conducted in parallel with the double-blind, placebo-controlled, core study (**Figure 2**)
  - Evaluating ITCA 650 60 mcg/day
  - Patients with T2DM on diet and exercise alone or with oral antidiabetes medications
- Objective: Evaluate the efficacy, safety, and tolerability of ITCA 650 in poorly controlled patients with T2DM
- Unless indicated for safety reasons, oral background treatment for type 2 diabetes was not modified

Figure 2. Study Flow Chart



INCLUSION CRITERIA

- Men or women age 18 to 80 years, inclusive
- Diagnosis of T2DM for ≥3 months prior to Screening
- HbA1c >10% but ≤12%
- Stable (≥3 months prior to Screening) treatment regimen of diet and exercise alone or in combination with a stable and optimal or near-optimal dose of:
  - Metformin, SU or TZD monotherapy, or any combination of the three
- Body mass index (BMI): 25 – 45 kg/m^2
- No prior treatment with GLP-1 receptor agonists

STUDY ENDPOINTS

Primary endpoint:

- Change in HbA1c between Week 39 and Day 0

Secondary endpoints:

- Change in body weight between Week 39 and Day 0
- Proportion of patients with an HbA1c <7% measured at Week 39
- Change in FPG between Week 39 and Day 0

Safety variables: AEs, hypoglycemic episodes, clinical laboratory measurements (chemistry, hematology, urinalysis, amylase, lipase, TSH and calcitonin), immunogenicity, 12-lead ECGs, vital signs, and physical examinations.

RESULTS

- Patient disposition (**Table 1**) and baseline characteristics (**Table 2**) are shown

Table 1. Patient Disposition (Safety Population)

	ITCA 650
Patients enrolled	60
Patients treated	60 (100%)
Treated with post baseline HbA1c result (mITT)	59 (98.3%)
Number who completed	52 (86.7%)
Number who discontinued prematurely	8 (13.3%)
Withdrawal by patient	1 (1.7%)
Adverse event	6 (10.0%)
Lost to follow-up	1 (1.7%)

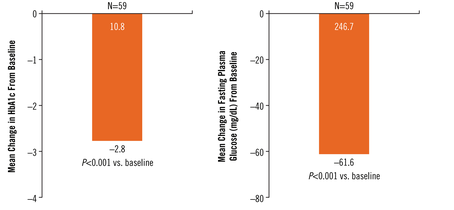
Table 2. Baseline Characteristics

Characteristic	ITCA 650 (N=60)
Age, years*	51.9 (10.2)
Duration of diabetes (yrs.)	8.9
Male, n (%)	34 (56.7)
Race, n (%)	3 (5%)
White	45 (75.0)
Black or African American	8 (13.3)
Other	5 (11.7)
HbA1c (%)	10.8 (0.7)
BMI, kg/m^2*	32.0 (4.9)
eGFR (mL/min/BSA)	95.5 (20.9)
Diet and exercise alone, n (%)	18 (30.0)
Diet and exercise + medication, n (%)	42 (70.0)

*Mean (standard deviation)

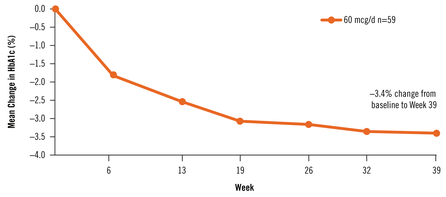
- ITCA 650 resulted in:
  - Significant reductions in HbA1c and FPG at 39 weeks (**Figure 3**)
  - A sustained reduction in HbA1c and FPG at each study visit (**Figure 4**)
  - A majority of patients with at least a 2% reduction in HbA1c (**Figure 5**)
  - A reduction in weight of 1.23 kg from mean baseline of 93 kg at 39 weeks (p=0.105 vs. baseline)

Figure 3. ITCA 650 Treatment Resulted in Significant Reductions in HbA1c and FPG over 39 weeks



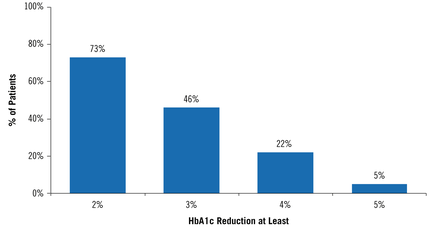
mITT Population

Figure 4. Reduction in HbA1c Over 39 Weeks



mITT Population

Figure 5. Majority of Patients Achieved ≥2% HbA1c Reduction

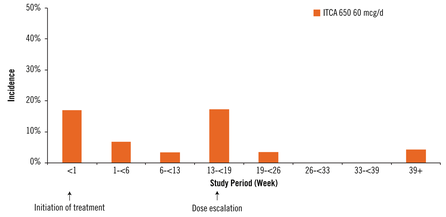


Only 2 (3.4%) patients had a HbA1c reduction ≤0.5%; 15 (25.4%) reached HbA1c ≤7.0%

Table 3. Incidence of Treatment-Emergent Adverse Events (Safety Population)

Preferred Term	ITCA 650 60 mcg/d (N=60)
Any Treatment-Emergent Adverse Event Leading to Permanent Discontinuation of Study Medication, n (%)	6 (10.0%)
Vomiting	3 (5.0%)
Diarrhea	1 (1.7%)
Nausea	1 (1.7%)
Sudden cardiac death	1 (1.7%)
Hyperglycemia	1 (1.7%)
Any Treatment-Emergent Adverse Event, n (%)	52 (86.7%)
Nausea	21 (35.0%)
Vomiting	16 (26.7%)
Diarrhea	14 (23.3%)
Application site hemorrhage	9 (15.0%)
Application site pain	4 (6.7%)
Upper respiratory tract infection	7 (11.7%)
Urinary tract infection	5 (8.3%)
Hypoglycemia	4 (6.7%)
Headache	5 (8.3%)
Hypertension	5 (8.3%)

Figure 6. Incidence of Nausea by Study Period (Safety Population)



SUMMARY

Efficacy

- Treatment with ITCA 650 20/60 mcg/d for 39 weeks in patients with high baseline HbA1c resulted in:
  - Clinically and statistically significant reductions in HbA1c from baseline
  - Mean weight loss of 1.23 kg; likely attenuated due to the correction of glycosuria with improved glucose control
  - 25% of these poorly controlled patients treated to HbA1c goal of <7%

Safety

- Treatment with ITCA 650 was well tolerated (**Table 3**); the most frequent AEs were consistent with the known profile of exenatide and those expected from a minor procedure (hematoma, bruising, bleeding)
- The most common treatment-emergent adverse events were nausea, vomiting, diarrhea, headache, URI and UTI; most were mild/moderate and diminished over time
- Events local to administration site were mostly mild, transient, occurring early after procedures, resolved without treatment, and rarely resulted in treatment discontinuation
- The incidence of nausea was <10% except for the week after mini-pump placement (**Figure 6**)
- No pancreatic events, thyroid cancer or major hypoglycemia
- All SAEs (4, 6.7%) were considered not related to study drug
- The incidence of minor hypoglycemia was 6.7%

CONCLUSIONS

- ITCA 650 at a dose of 60 mcg/day resulted in clinically significant glycemic control and was well tolerated in patients with T2D and elevated baseline HbA1c of >10.0% and ≤12.0%
- Statistically and clinically significant reductions of HbA1c and FPG were observed and maintained during 39 weeks of treatment
- The most common adverse events were consistent with the known effects of exenatide and a minor office procedure; were most commonly observed early in the course of treatment and improved over time
- The results of this study supports treatment with ITCA 650 60 mcg/day for patients with higher HbA1c and additional clinical development of ITCA 650 in patients with T2D and poor glycemic control

FREEDOM-1 HBL