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Evaluation of a New Placement System for ITCA 650

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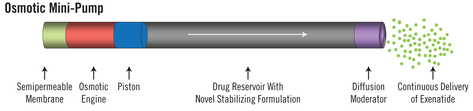
INTRODUCTION

- Poor adherence to therapy is common with all antidiabetes drugs (Flory et al, 2017) and is associated with inadequate glycemic control, poor outcomes, and increased healthcare resource utilization (Currie et al, 2012; DiBonaventura et al, 2014).
- Novel therapeutic approaches for treating type 2 diabetes are needed that provide improvement in adherence.
- ITCA 650 is an investigational drug device combination product that consists of an osmotic mini-pump that delivers exenatide subcutaneously for extended periods of time. Three and 6 months pumps were evaluated in the ITCA 650 Phase 3 Clinical program (**Figure 1**).

Figure 1. ITCA 650 Osmotic Mini-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 that forces the drug formulation to be released through the orifice of the diffusion moderator.
- In Phase 2 and 3 clinical trials, ITCA 650 significantly reduced glycosylated hemoglobin and body weight in patients with type 2 diabetes who had an inadequate response to oral antidiabetic agents (Henry et al, 2013; Baron et al, 2015, Rosenstock et al, 2016).
- ITCA 650 is placed subdermally in the abdominal wall using a Placement Tool during a brief clinic visit by healthcare providers who successfully completed an Intarcia training program.
- If the ITCA 650 is placed deeper than the subdermis (into the subcutaneous fat) removal of the device may become difficult.
- In order to limit the depth of placement of the ITCA 650 mini-pump, a Placement Guide (depth guide) that interfaces with a Placement Tool was developed.
- This study evaluated whether the addition of the Placement Guide to the Placement tool (together called the Placement System), enabled consistent and shallow subdermal placement of an ITCA placebo osmotic mini-pump at a depth that facilitated easy removal.

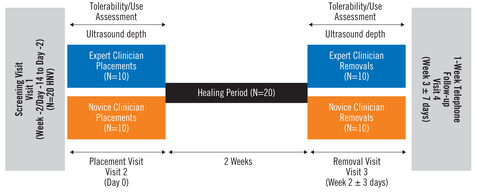
[NEW LINK TO BE PROVIDED]

METHODS

Study Design

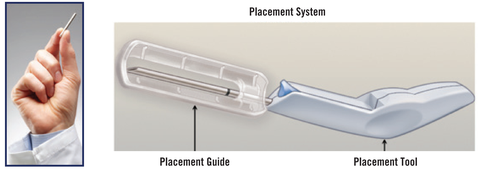
- This was a Phase 1, open-label, single-site study (**Figure 2**).
- All subjects received an ITCA placebo osmotic mini-pump that looked identical to the ITCA 650 osmotic mini-pump used in the Phase 3 program.

Figure 2. Study Design



- Primary objective:
  - Assess the ability of the clinician to correctly use the Placement System to consistently place the osmotic mini-pump (**Figure 3**) in the subdermis of the abdominal wall at a depth that facilitates easy removal of the mini pump.
- Secondary objectives:
  - Assess clinician's ability to remove osmotic mini-pump.
  - Assess procedural tolerability.
  - For experienced clinicians, assess ease of use of the Placement System based on previous experience with the Placement Tool alone.

Figure 3. ITCA Placebo Osmotic Mini-pump (left) and Placement System – Placement Tool and Placement Guide (right)



Subject Selection

- Healthy adults ages 18 to 60 years inclusive and body mass index of 25 to 40 kg/m^2 inclusive
- Subjects were excluded for:
  - Use of anticoagulants or >1 aspirin (325) mg daily for the week prior to enrollment
  - History of hemophilia or other bleeding disorder
  - History of skin disorders that could interfere with placement or removal procedures

Criteria and Definitions for Clinician Selection

- Office-based healthcare professionals (HCPs) e.g., Physician [MD or DO], Physician Assistant [PA] or Nurse Practitioner [NP]
- All HCPs had ≥2 years of professional experience:
  - Novice Group (N=2)
    - No prior experience with placement and removal procedures with osmotic mini-pumps
  - Experienced Group (N=2)
    - Performed ≥10 placement and removal procedures of the osmotic mini-pumps using the Placement Tool in ITCA 650 clinical studies

Study Procedures

- Subjects underwent subdermal placement of the osmotic mini-pump in one quadrant of the abdominal wall using the Placement System.
- Subdermal depth of the osmotic mini-pump was verified by ultrasound by a single certified ultrasound technician.
- Each clinician performed all placement and removal procedures for 5 subjects.
- Following a 2-week period to allow the incision to heal, each subject returned (Visit 3) for a repeat ultrasound.
- Osmotic mini-pump was removed, in accordance with the instructions for use (IFU), after the second ultrasound on Visit 3.
- Subjects were given post discharge instructions for incision care.
- Subjects received a follow up telephone call 7 days following removal.

Study Assessments

- All clinicians were asked scripted questions regarding their impressions of the Placement System before the Placement Session and completed a written questionnaire and survey after the Placement Session.
- The time that the clinicians took to place and remove the ITCA 650 placebo mini-pump was assessed as the time from incision until the last Steri-Strip was affixed.
- Adverse events (AE) occurring at the placement/removal site and/or reported during the procedure were collected.

Study Analysis

- Primary endpoint was the number and percent of correct placements of the osmotic mini-pump by each clinician group.
- Secondary endpoints were:
  - Number and percent of placements that were correctly removed
  - Mean depth and consistency of depth of placement
  - Time for placement and removal (time from incision until Steri-strip affixed)
  - Clinician's assessment of ease of use and important features
  - Safety and tolerability

RESULTS

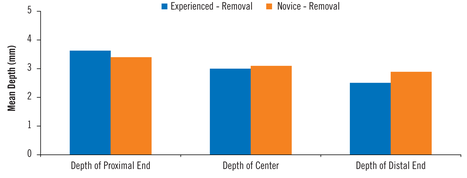
Table 1. Subject Disposition and Characteristics

Screened	23 (100%)
Enrolled and completed	20 (87%)
Male:female	11 (55%) 9 (45%)
Mean (SD) age, years	35.7 (9.4%)
Mean (SD) body mass index, kg/m^2	30.4 (3.9%)
Race, n (%)	
White	12 (60%)
Black/African American	4 (20%)
Asian	1 (5%)
Other	3 (15%)

Analysis of Placement and Removal Procedure

- Osmotic mini-pumps were correctly placed in all 20 subjects, regardless of clinician experience.
- Novice Group: Osmotic mini-pump was correctly removed in 10 subjects (100%).
- Experienced Group: Osmotic mini-pump was correctly removed in 9 subjects (90%).
  - During the manual manipulation and immobilization in preparation for device removal, the osmotic mini-pump was extruded in 1 subject
- Depth of placement of the osmotic mini-pump was similar between Clinician Groups at the time of removal (Week 2) (**Figure 4**).
- The depth of subdermal placement measured by ultrasound on Day 0 is likely to be overestimated because of tissue swelling due to lidocaine injection.

Figure 4. Depth for ITCA Placebo Osmotic Mini-pump (N=20) at Week 2



Procedural Characteristics

- All osmotic mini-pumps were placed in the left upper abdominal quadrant.
- Mean (SD) placement time was 12.9 (2.5) minutes in the Experienced Group and 12.1 (2.3) minutes in the Novice Group.
- Mean (SD) removal time was 6.8 (3.5) and 9.9 (4.6) minutes in the Experienced and Novice groups, respectively.
- All osmotic mini-pumps were placed within 17 minutes and removed within 16 minutes.

Physician Survey Results

- Most clinicians agreed that the Placement System was easy to use, were confident in its use, felt the user instructions were clear and useful, and that the depth of the placed osmotic mini-pump allowed simple, easy removal.
- ≥90% of responses in the Experienced and Novice clinician groups felt that the osmotic mini-pump removal procedure was simple and easy, and that the IFU were clear and useful.
- Both Clinician Groups verbalized that the IFU for placement and removal of the mini-pump using the Placement System was clear and were confident using the system.
- Both groups also indicated satisfaction with the placement depth and had no procedural safety concerns.
- The Experienced Group expressed preference for the use of the Placement System over previous use of the Placement Tool alone.

Safety Evaluation

- 1 subject in the Experienced Clinician Group experienced an AE of device extrusion just prior to the removal procedure.
  - AE was mild in severity
- No serious AEs, clinically significant AEs or discontinuation for AEs.
- No clinically significant laboratory or physical examination findings were seen.

CONCLUSIONS

- The ITCA 650 Placement System enabled the consistent and appropriately shallow subdermal placement of the osmotic mini-pump at a depth that facilitated easy removal in all subjects regardless of the clinician's prior experience with the placement/removal procedures.
- The Placement System limits the depth of placement of the osmotic mini-pump and has the potential to mitigate the risk of deep placement of the device.
- The experience of HCPs showed that ITCA 650 was easy to place and remove, and that HCPs can be trained with a simple set of instructions to perform these procedures.
- Based on these data the Placement System was introduced into the ITCA 650 clinical studies and has been successful at limiting the deep placement of devices in the subcutaneous fat.

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