ORIGINAL RESEARCH

Summative Usability Evaluation of the SCTE-AI Device: A Novel Prefilled Autoinjector for Subcutaneous Testosterone Administration

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ABSTRACT

Background: The subcutaneous testosterone enanthate (TE) autoinjector (SCTE-AI) is a single-use, pre-filled, disposable autoinjector intended for testosterone (T) self-administration in adult males with T deficiency.

Aim: To evaluate the usability of the market configuration of the SCTE-AI, including packaging and instructions for use (IFU), in order to identify and mitigate any preventable patterns of use errors that could result in harm.

Methods: 4 groups of participants (injection-naïve or injection-experienced patients or caregivers) were randomized to 1 of 3 doses (50, 75, and 100 mg) of TE and either trained (ie, reviewed the IFU and shown how to properly inject) or not trained (only given the IFU). After simulated at-home use, participants were asked questions regarding the comprehensibility of the IFU and the intuitiveness/usability of the device. All tasks were measured as success, use error, or close call (participant initiated an error but recovered in time).

Main Outcome Measure: Usability (success rates, errors, and close calls) of the drug/device combination by adult males with T deficiency or their caregivers.

Results: 65 patients received 1 dose of TE, and 59 patients received 2 doses. Overall, 99 of 123 (80.5%) attempted injections resulted in administration of 1 full dose. Injection success rates were high and comparable among the various user groups. The most common use error (21 of 24) was due to not holding the autoinjector on the abdomen long enough (at least 8 seconds). Few critical drug delivery and safety errors or close calls were observed. No unmitigated use errors by patients or caregivers were apparent that could result in harm or have a negative impact on treatment. SCTE-AI was well tolerated.

Clinical Implications: The SCTE-AI development process resulted in a subcutaneous, TE autoinjection device that is intuitive to use, with clear labeling and packaging and an easy-to-understand IFU, providing an option for T-deficient adult males to self-inject subcutaneously at home.

Strength & Limitations: The strengths of the study include use of a patient-ready drug/device combination for self-administration and inclusion of both injection-naïve and injection-experienced patients and caregivers. The main limitation of the study is the presence of observers/cameras that may have distracted or created performance anxiety, potentially contributing to errors.

Conclusion: Results of this usability validation study indicate that the SCTE-AI device is safe and intuitive to use, with a low potential for harm and is associated with a high rate of injection success, regardless of prior training or experience. **Arora S, Moclair B, Murphy K, et al. Summative Usability Evaluation of the SCTE-AI Device: A Novel Prefilled Autoinjector for Subcutaneous Testosterone Administration. J Sex Med 2018;XX:XXX–XXX.**

INTRODUCTION

Testosterone deficiency (TD) is a major medical condition that negatively affects male sexuality, reproduction, general health, and quality of life.[1] Patients with TD, also known as *hypogonadism*, typically suffer from diminished sexual function, decreased muscle strength, fatigue, and depression.[1,2] TD has a negative impact on male physical function by reducing muscle

mass and strength and negatively affects sexual aspects of quality of life by reducing libido, decreasing erectile and orgasmic function, and compromising overall sexual activity.[1,3]

Patients with TD are treated with testosterone (T) replacement therapy, with the goal of restoring T to physiological levels. When achieved, patients experience improved mood, increased bone mineral density and muscle mass, reduced adiposity, and improved libido and sexual function.[4–8] Current approved T therapies in the United States include intramuscular (IM) injections, transdermal, transbuccal, and intranasal applications, and implantable pellets. In addition to challenges in providing steady serum levels of T, each is associated with some limitations (eg, inconvenience, pain, cost) that has an impact on patient compliance.[2,9–11]

Transdermal disadvantages include transference, that is, T possibly transferred to others via skin-to-skin contact and the application of 2 patches daily due to serum T levels in the low-normal range in some androgen-deficient men.[2,11] Transbuccal disadvantages include gum-related adverse events (AEs) in 16% of treated men.[2] Disadvantages of implantable pellets include the requirement for surgical incision; pellets may extrude spontaneously, and the lack of control of a patient's exogenous T dose during the implanted time interval[2,11] can be problematic.

The subcutaneous T enanthate (TE) autoinjector (SCTE-AI) is a novel single-use, prefilled, disposable auto-injector intended for at-home self-administration of T in adult males with TD.[12] SCTE-AI has been demonstrated in a phase 2 trial to be safe and efficacious, providing predictable, reproducible, and dose-proportional T levels with acceptable levels of tolerability.[12] SCTE-AI provides patients and caregivers with a convenient alternative to current U.S. Food and Drug Administration–approved T formulations requiring topical or IM administration.

The U.S. Food and Drug Administration has implemented guidance for usability and human factors regarding the evaluation of medical devices during the design process, requiring end-user involvement during this process when reviewing market presubmission.[13] The overall aim of the guidance is to improve the design of devices to minimize potential use errors and resulting harm. A successful usability and human factors validation is achieved when no patterns of preventable use errors are detected for critical tasks, defined as a user task, which if performed incorrectly or not performed at all, would or could cause serious harm to the patient or user, in which harm is defined to include compromised medical care.[13] In summary, usability testing is essential to the design, clinical validation, regulatory approval, and widespread implementation of new medical devices.[14]

During the course of SCTE-AI development, results from prior autoinjector device usability studies guided progressive improvement in device design, packaging, labels, and instructions for use (IFU). Earlier usability studies include the use of simulated injection devices (N = 94), as well as injection of oil-filled placebo devices into prosthetic belly pads (N = 55) (Antares, data on file). The final SCTE-AI drug/device combination has been used as an investigational TD therapy for more than 2 years in clinical and human factors studies. The goal of this summative usability study is to evaluate this current version of the SCTE-AI in terms of packaging design, product labeling, and IFU to ensure that any preventable patterns of use errors have been mitigated by minimizing patient and caregiver use difficulties. Reduction of preventable use errors should minimize any harm and maximize usability of the SCTE-AI drug/device combination.

## MATERIALS AND METHODS

Product Description and Use

SCTE-AI is a USP-grade T formulation provided in a pre-filled, unit-dose, autoinjector delivery system. The single-use disposable autoinjector consists of a plastic body with on-device labeling and a viewing window (the window allows end users to see the contents of the inner drug chamber) as well as a needle guard and a cap (Figure 1A). After removing the cap, the end user places the needle end of the auto-injector device against a gathered area of abdominal skin at a 90°angle and firmly pushes the autoinjector down on the abdomen injection site. Once the needle end of the device has been pushed down all the way, the user continues to hold down after a "click" is heard, allowing the T to be injected subcutaneously into the patient.

User-Group Definitions

"Injection-naïve" patients or caregivers have never injected using a needle and syringe or any form of pen, jet, or related medication autoinjector. "Injection-experienced" patients or caregivers have administered injections using a needle and syringe or any form of pen, jet, or related medication auto-injector at least 3 times. A subgroup of patients and caregivers were given one-on-one training prior to their first injection. Participants were trained to use the device correctly by simulating an injection with the training device (not containing TE). The participants then performed their first injection. In an actual-use setting, there is typically no learning decay for the first use of this device. After a week, the participant returned and performed a second injection using the TE device (or the caregiver performed an injection on the participant with hypogonadism). In order to evaluate learning decay for this device, no further training was given before the second injection.

Study Design

The summative usability evaluation of the SCTE-AI was designed to present the end-user population (injection-naïve and injection-experienced patients and caregivers) with a use scenario involving the active product under simulated actual-use
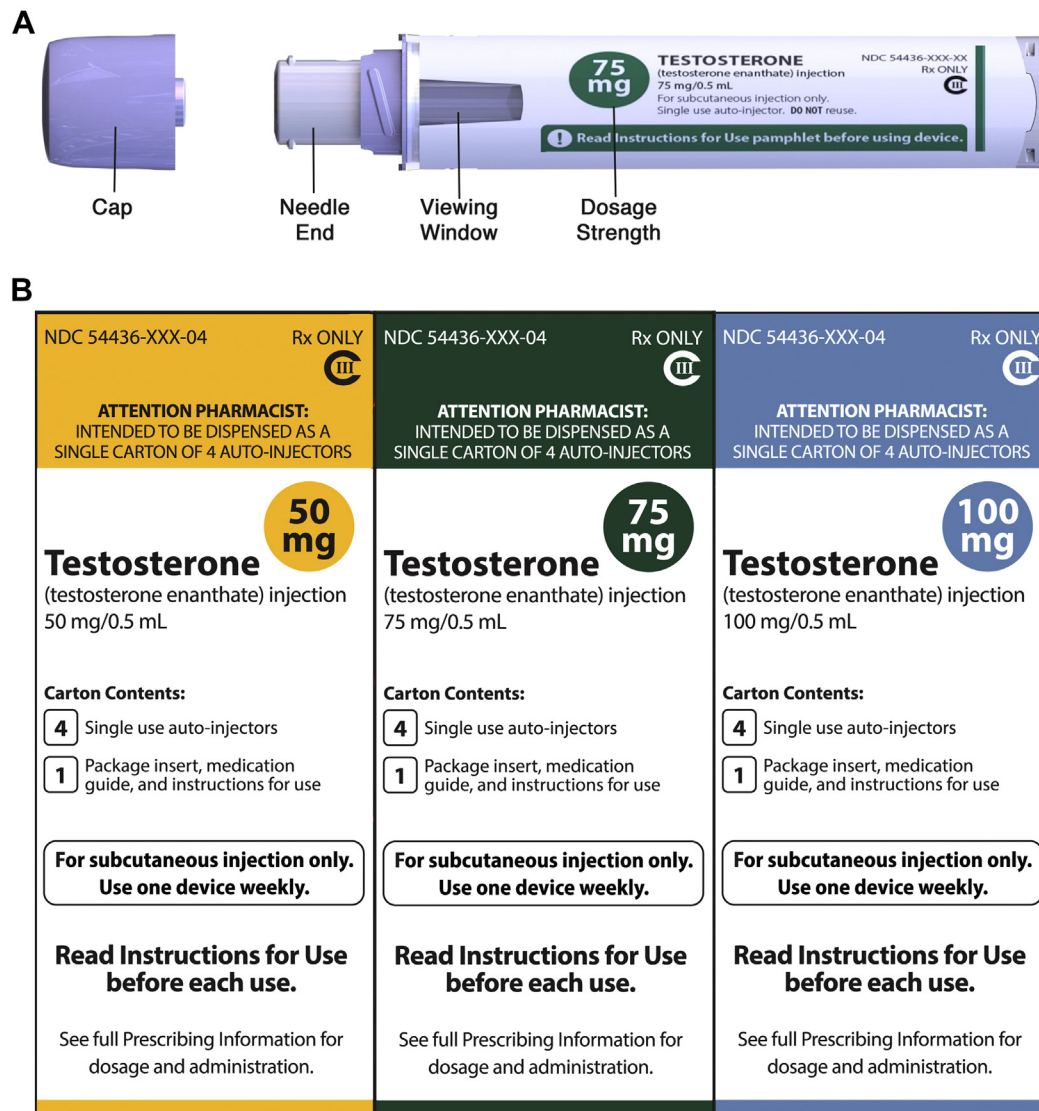
Figure 1. A, Diagram of the parts of the subcutaneous testosterone enanthate autoinjector device. Image obtained from the instructions for use. B, Subcutaneous testosterone enanthate autoinjector packaging for the 3 different testosterone enanthate dose levels (50, 75, and 100 mg).

conditions (ie, a simulated home environment at 3 different testing sites). Each study session included dedicated usability evaluation steps to ensure the study staff systematically assessed device usage, with the objective of identifying errors and close calls (defined as an error made during use, but the task is continued and the error is corrected any time before completing the use process). Direct observations were made as well as audio/video recordings.

Study participants (patients or caregivers) were randomized to trained and untrained groups and instructed accordingly. Patients were then randomized to 1 of 3 doses (50, 75, and 100 mg) of the active drug TE. Participants were asked to select their dose in order to test the differentiation among the 3 different dose packages (Figure 1B). Visit 1 was screening, while visits 2 and 3 were for the first and second injections, respectively. The participant's first visit was a dedicated screening visit, whereupon the participant was screened for verification eligibility as per the clinical protocol and usability protocol for inclusion/exclusion criteria. On the second visit, participants were asked to use the device as they would in their homes and as if staff were not present. Subsequently, staff asked questions regarding the comprehensibility of instructional materials accompanying the product, the intuitiveness/usability of the device, and around the elements of the device (eg, autoinjector activation). If use errors/close calls were observed, patients and caregivers were interviewed to determine the root cause of the participant's understanding about the use of the product and his choice whether or not to read the IFU. Participants then were asked to return to the study site a week later in order to perform a second injection after a week of learning/training decay.

Study Participants

The study was conducted in accordance with the Declaration of Helsinki and with all applicable laws and regulations of the region and country where the study was conducted and was in compliance with Good Clinical Practice Guidelines. Informed consent was obtained from all study participants. Men ≥18 years of age were eligible for inclusion if they had a documented history of TD, were in good health as determined by the investigator and based on medical history, physical examination, vital signs, electrocardiogram (ECG), and clinical laboratory tests. Patients (caregivers) had to be able to speak, read, and understand the English language at a sixth grade reading level or higher. Patients or caregivers were also required to be willing to have photographs taken and/or be video recorded while they completed study tasks. Images were de-identified prior to any potential use of the image(s) for scientific or educational purposes.

Laboratory Tests, Biomarker Analyses, and Safety Analyses

Safety assessments were conducted in the safety population (defined as all patients who were randomized and took at least 1 dose of investigational product [IP]) at scheduled intervals during the study, including adverse drug reactions, injection site assessments, clinical laboratory measurements (biochemistry profile, hematology, coagulation, urinalysis, and PSA levels), physical examinations, vital signs and 12-lead ECGs.

Statistical Analyses

Demographic and baseline characteristics were summarized descriptively. Age and body mass index were summarized by patient count, mean, and SD. Categorical variables (race, ethnicity, and prior T therapy) were summarized by the number and percentage of patients in the corresponding categories. AEs were coded using the *Medical Dictionary for Regulatory Activities*. A treatment-emergent AE (TEAE) was defined as an AE that started on or after the first dosing of IP or existed prior to the first dose and worsened in severity or relatedness to the IP after dosing. An adverse drug reaction was defined as a TEAE that was considered by the investigator to be related to the IP. Postdose injection site assessments were performed at visits 2 and 3. Injection site parameters evaluated included erythema, induration, bleeding, hematoma, ecchymosis, presence of pinprick or needle mark, pressure mark, itching, and pain.

RESULTS

Injection Success Rates, Overall and by User Groups

Overall, 65 study participants meeting all inclusion/exclusion criteria received 1 dose of SCTE-AI (safety population). Demographics, baseline characteristics, and user groups are shown in Table 1. More than 90% (59/65) of participants were administered 2 doses. SCTE-AI lay users were evenly distributed into 4 groups:

Table 1. Demographics, baseline characteristics, and participant user groups

Demographics	Overall (N = 65)
Age at informed consent (y)	
Mean (SD)	55.3 (8.98)
Ethnicity—n (%)	
Hispanic or Latino	1 (1.5)
Not Hispanic or Latino	64 (98.5)
Race—n (%)	
White	48 (73.8)
Black or African American	17 (26.2)

Baseline characteristics	n (%)
Body mass index (kg/m^2) at screening—mean (SD)	30.12 (5.117)
Not currently receiving T therapy	55 (84.6)
Currently receiving T therapy	10 (15.4)
IM or SC testosterone injection	8 (12.3)
Topical/transdermal testosterone therapy	1 (1.5)
Testopel	1 (1.5)

User groups	Randomized, first injection	Both injections
Injection-naïve patient	16	15
Injection-experienced patient	15	15
Injection-naïve caregiver	15	14
Injection-experienced caregiver	19	15
Total	65	59

Abbreviations: IM = intramuscular; SC = subcutaneous.

injection-naïve patients (n = 15), injection-experienced patients (n = 15), injection-naïve caregivers (n = 14), and injection-experienced caregivers (n = 15). All tasks were measured as a success, close call, or use error. Success is defined when a participant completes a task or use scenario without committing an unrecoverable use error. A use error is defined as a user action or lack of user action while using a medical device that leads to a different result than that intended by the manufacturer or expected by the user.

Injection success rates were high and comparable among the various user groups (Figure 2A and 2B): patients (84.8% and 86.2% for the first and second injections, respectively), caregivers (86.2% and 85.9% for the first and second injections, respectively), injection-naïve (85.6% and 85.4% for first and second injections, respectively), and injection-experienced (85.4% and 86.5% for the first and second injections, respectively). No significant differences in terms of total error and close call rates for both the first and second injections were observed between patient and caregiver users (first injection, 15.2% vs 13.8%; second injection, 14.0% vs 14.1%, respectively) and between injection-naïve and injection-experienced users (first injection, 14.4% vs 14.6%; second injection, 14.6% vs 13.5%, respectively). Patients were asked, "How would you describe your experience using the device?" (A scale of 1−7 was used; 1 rated as unclear and 7 rated as very clear.) 60 patients or caregivers gave an average rating of 6.4.
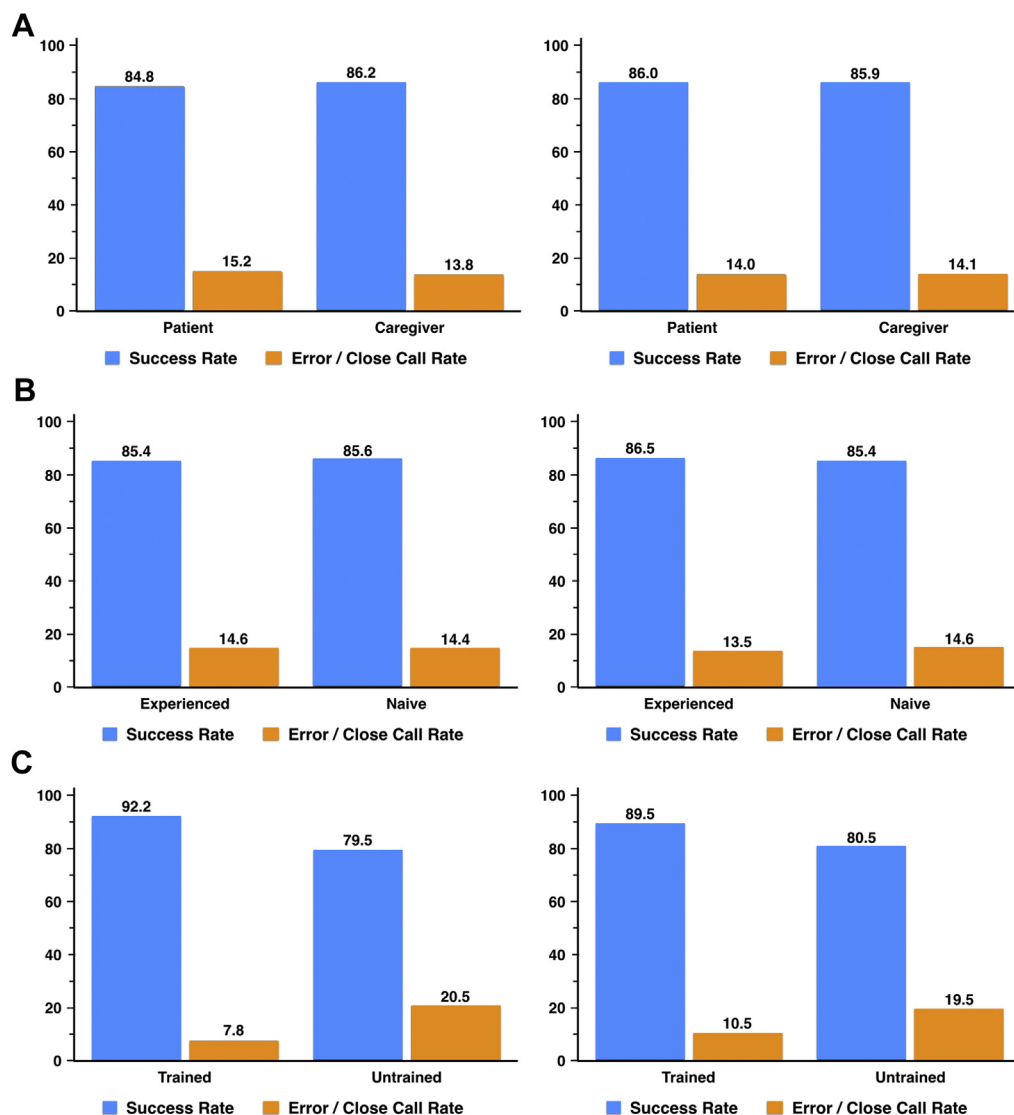
Figure 2. A, Patient vs caregiver error and close call rates for the first and second injections. B, Experienced vs naïve error and close call rates for the first and second injections. C, Trained vs untrained use error and close call rates for the first and second injections.

Trained participants scored higher injection success rates than untrained participants for the first injection (92.2% vs 79.5%, respectively), as well as for the second injection (89.5% vs 80.5%, respectively) (Figure 2C). As expected, trained participants had lower total errors and close call rates compared to untrained participants for both the first and second injections (first injection, 7.8% vs 20.5%; second injection, 10.5% vs 19.5%, respectively) (Figure 2C). Among trained participants, higher error/close call rates were observed on the second injection, likely due to training decay (first injection, 7.8%; second injection, 10.5%).

Completion of Critical Tasks: Delivery of Appropriate Dose

In 123 attempted injections, 99 (80.5%) resulted in administration of 1 full dose. A hold time of 8 seconds and above ensures full dose delivery, while a 10-second hold time is intended to provide a safety margin for full dose delivery should a patient be unable to detect or interpret device cues related to injection initiation and completion. The most common reason for not delivering a therapeutic dose was not holding the device in place for at least 8 seconds (19 users/21 injections; 12 use errors for the first injection/9 for the second injection) (Figure 3). The average user hold time for the first injection during the study was 10.42 ± 4.78 seconds, and the average hold time for the second injection was 10.27 ± 4.41 seconds. Of the 21 injections (of which 10 were patients and 11 were caregivers) that were not held for at least 8 seconds (short injections), participants spoke of gauging dose delivery using either the second click or the color change for 7 injections that were held for either 6 or 7 seconds. For the second injection, 28 use errors and no close calls were reported; 14 patients and 14 caregivers did not hold the device for 10 seconds. During the second visit, users were asked, "How
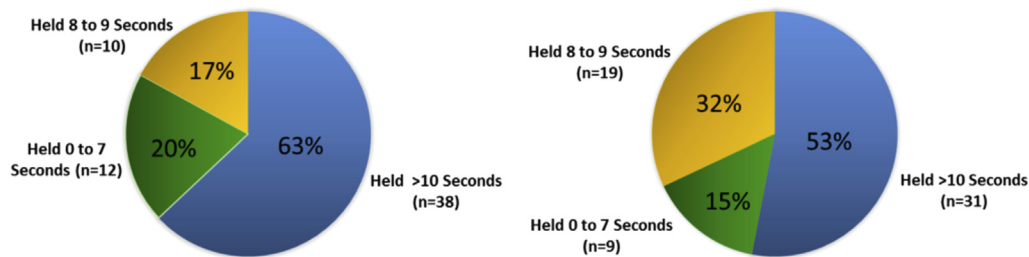
Figure 3. First and second injection hold times by study participants (% of total users). The majority of injection hold times were >10 seconds for each injection. The average user hold time for the first injection during the study was 10.42 ± 4.78 seconds, and the average hold time for the second injection was 10.27 ± 4.41 seconds.

clear is it from the instructions for use what you need to do to allow complete injection of the drug when administering the injection?" All 59 study participants rated the instructions a 5, 6, or 7 (a scale of 1–7 was used; 1 rated as unclear and 7 rated as very clear), with an average rating of 6.8. Overall, participants rated the IFU a 6.8 out of 7 on clarity of holding for 10 seconds.

During the study, 2 use errors and 1 close call were observed regarding checking the window after dose delivery. Of these 3 instances, 2 users delivered a full dose and only failed to check the window during

1 of their 2 injections, while the third user did not deliver a full dose during the first injection, nor did they check the window after delivery—but both delivered a full dose during their second injection and checked the window. Only 1 participant failed to remove the autoinjector cap; this user (patient self-administered) did not read the instructions prior to attempting the injection. Close calls (9) were observed (no errors) related to users not pushing the autoinjector down against the injection site until a "click" was heard. In all 9 cases, users were able to self-correct and actuate the device. Selecting the appropriate dose was not considered a critical task (and unlikely to occur in the real world); nevertheless, it is noteworthy that 1 user (patient) selected the incorrect dose and did so knowingly in order to receive the highest dosing strength.

Another critical task associated with delivery of an appropriate dose included checking the expiration date. Use errors (35) and

close calls (2) related to checking the expiration date occurred; 18 of those errors were due to users assuming they would be provided with drug that was not expired and valid for the whole expected dosing period, and 11 errors were related to users forgetting to check the expiration date.

Completion of Critical Tasks: Safe Delivery

Referring to the IFU (see Supplementary Appendix) is considered a critical task associated with safe drug delivery. Of the 64 study participants who administered a first injection, 34 (53%) referred to the IFU without any prompting by the study moderator before or during their first injection. Of the 59 study participants who administered a second injection, 35 (59%) referred to the IFU without any prompting by the study moderator before or during their second injection. Regarding the impact of reading the IFU prior to administering the first injection on injection success rates in the trained vs untrained groups, success rates were highest in trained users, whether they read the IFU (92.2%) or did not read the IFU (91.0%), while success rates were lowest in untrained users who did not read the IFU (70.1%) (Figure 4). Patients and caregivers were asked, "How would you describe the instructions for use for helping you to use the device?" (A scale of 1–7 was used; 1 rated as unclear and 7 rated as very clear.) 60 patients or caregivers gave an average rating of 6.6. Success rates were lower in untrained users who either read the IFU (80.5%) or who did not read the IFU (70.1%). From a clinical perspective, these results suggest
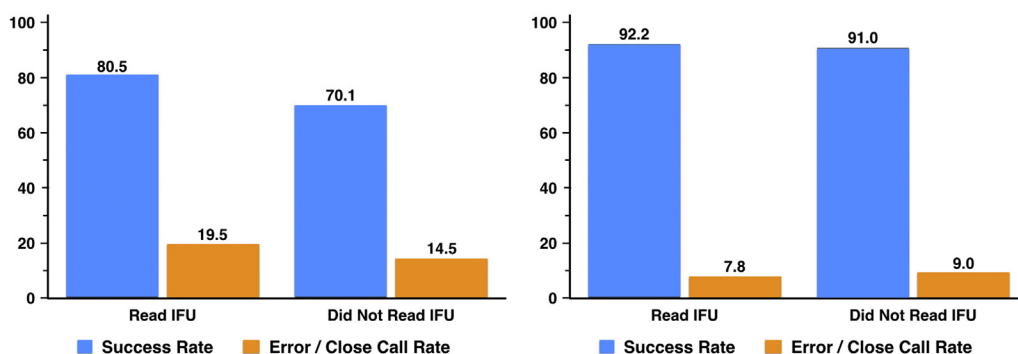
Figure 4. Use error and close call rates for untrained users (left) or trained users (right) who read the instructions for use vs users who did not read the instructions for use. Both left and right panels show first injections.

that it is ideal for each newly prescribed patient to be provided with first use in-office specific training on how to use the SCTE-AI.

The current directions instruct users to dispose of the used device in either a sharps container, or as per local laws permit in a rigid, sealable, puncture- and leak-resistant household container. There were frequent errors (46) and close calls (3) regarding disposal, whereby users wanted to throw the device in the regular trash. The 2 most common causes for improper disposal were (1) users are accustomed to throwing used unwanted items in their regular trash (tended to persist from the first to second injection) and (2) oversight, wherein users were not sure where to dispose of the device (declined from the first to second injection). During the second visit, patients were asked, "How clear is it from the instructions for use how the device needs to be disposed?" (A scale of 1–7 was used; 1 rated as unclear and 7 rated as very clear.) 59 patients or caregivers gave an average rating of 6.7.

Adverse Events, Injection Site Reactions and Pain Assessment

Based on the evaluation of AEs, clinical laboratory variables, vital signs, ECG readings, and physical examination findings, treatment with the SCTE-AI was well tolerated in this patient population. In total, 5 (7.7%) patients experienced a TEAE during the study. All TEAEs were considered to be mild or moderate; no patient had a TEAE that was considered to be severe. The most common system organ class of TEAEs were skin and subcutaneous tissue disorders (3 [4.6%] patients); cardiac disorders (1 [1.5%] patient); ear and labyrinth disorders (1 [1.5%] patient); and respiratory, thoracic, and mediastinal disorders (1 [1.5%] patient). No 1 TEAE (preferred term) was more frequently reported than any other TEAE.

Overall, 1 (1.5%) patient had a TEAE (urticaria) assessed by the investigator as causally related to the IP. The TEAE of urticaria (system organ class of skin and subcutaneous tissue disorders) was considered to be mild in severity and occurred at the administration of the first dose of the IP by an injection-naïve caregiver, who experienced issues with IP administration and persisted for a duration of 4 days. The circumstances of the first dose administration in conjunction with the observations of event duration, lack of accompanying itch, and lack of recurrence with the second injection, make it unlikely that hypersensitivity to the IP was the cause of the event. No patient experienced a treatment-emergent serious AE. No patient had a TEAE that led to discontinuation from the study, and no patient had an event of pulmonary oil microembolism or anaphylaxis during the study. No patient had any AE that led to death during the study. The majority of clinical laboratory parameters, vital signs, and physical examination findings were unremarkable. The magnitude of the effect on blood pressure at study visits was, on average, modest.

Subcutaneous injection of TE via the autoinjection device was well received by patients. Overall, no patients had injection site observations of bleeding, hematoma, ecchymosis, or pain. Less than 10% of patients had injection site observations of erythema, induration, or itching. More than 10% of patients had injection site observations of pinprick/needle mark (27 [41.5%] patients) and pressure mark from the needle guard (14 [21.5%] patients). Overall, only 3 (4.6%) patients experienced an injection site reaction ≥25 mm in diameter (or smaller if accompanied by itching), and no patients experienced pain. For the category of erythema, 2 (3.1%) patients experienced an observation >25 mm in diameter. For the category of induration, 1 (1.5%) patient experienced an observation >25 mm in diameter.

DISCUSSION

In using the SCTE-AI, patients with TD and their caregivers demonstrated a high rate of injection success for each injection (patients, 84.8–86.0%; caregivers, 86.2–85.9%) (Figure 1A). Similar injection success rates occurred whether or not patients or caregivers had injection experience (Figure 1B). Differences were noted in success rates depending on whether or not prior training had taken place; training prior to the first injection yielded a comparable injection success rate between the first and second injections where training decay likely did not factor, and was expectedly higher than in untrained participants (Figure 1C). Reading the IFU improved success rates on untrained participants, while success rates of trained participants who read the IFU did not improve more than those who did not read the IFU (Figure 4).

Patients may face barriers to adherence of T replacement therapy—factors that contribute to adherence include convenience, level of discomfort or pain, and patient satisfaction with the delivery system.[15] In the primary clinical study, patients using the SCTE-AI drug/device were highly adherent to the dosing regimen, indicated a virtually pain-free experience, and demonstrated a high degree of satisfaction with the SCTE-AI (primary phase 3 trial, manuscript accepted for publication). The SCTE-AI conveys advantages over other modes of T administration. There is no risk of secondary exposure as with gels and theoretically less risk of pulmonary oil embolism, as has been reported with higher volume IM T in oil injection.[16] The option for patients to self-inject subcutaneously in the comfort of their own homes provides a much greater level of convenience compared to T delivery by IM injection.[17]

The main user error resulted in delivery of an incomplete dose of T. A hold time of 8 seconds or more ensures full dose delivery, with a suggested time frame of 10 seconds after the "click" is heard; this information is provided in the IFU as an overstatement of how long the injection takes in order to encourage users to administer for an adequate amount of time. The 10-second hold time is intended to provide a fail-safe method, should a user be unable to detect or interpret device cues related to the initiation and completion of the injection. Importantly, delivery of less than a full dose does not pose life-threatening or serious harm. The average SCTE-AI device delivery time is

<8 seconds. Therefore, the success rate of >80%, based on a hold of ≥8 seconds, was likely an underestimation of the rate of full T dose delivery. Moreover, the self-administration experience with weekly dosing of SCTE-AI would likely provide an opportunity to improve and master injection skills. Proper disposal of the autoinjector into a sharps container prevents potential exposure to bloodborne pathogens to caregivers or family members. It is difficult to have an impact on patient behavior regarding proper disposal, particularly if they are unaware of the risks of used needles. As a result of this, the design of the SCTE-AI includes a safety shield lock-out mechanism has been designed into the SCTE-AI device that prevents users from needle exposure after the dose delivery.

This usability study represents the fifth iteration of human factors testing for the SCTE-AI drug-device combination. Each successive test resulted in alterations to the packaging, device labelling, and/or IFU to address sources for use errors. In the discussion of use errors detected in this study, patients or caregivers seldom note the packaging, label format, label content, IFU format, or contents as the source of their misapprehension of proper procedure. Rather, the discussion provided by users uniformly cites prior practices, beliefs, or memory lapses.

Based on the evaluation of AEs, clinical laboratory variables, vital signs, ECG readings, and physical examination findings, treatment with SCTE-AI was well tolerated in this patient population. No deaths, serious AEs, or pulmonary oil microembolism occurred during the study. Postinjection observations were minor in nature and reflected the skin's response to being pierced with a needle, and no patients reported pain after administration via the SCTE-AI.

Strengths of the study include use of a patient-ready drug/device combination for self-administration in a simulated home-use environment, rather than injection pads or mock devices. Another strength is the study design; inclusion of injection-naïve and injection-experienced patients and caregivers is representative of real-world user groups consisting of patient self-administration or caregiver-assisted injections with no prior injection experience. Study limitations include the presence of observers/cameras that may have distracted patients/caregivers and may potentially contribute to errors (ie, performance anxiety); some participants may have performed better without an observer present and as a result, become more relaxed/comfortable. Known as the "observer effect," this effect has been shown to have an impact on results.[18] This unwanted effect is difficult to avoid in observational human usability studies and could be viewed as helping success rates because patients may try hard to perform correctly.

These results show that the development process for the SCTE-AI resulted in a subcutaneous, T auto-injection device that is intuitive to use, with clear labeling and packaging and an easy-to-understand IFU. Few critical drug delivery and safety errors or close calls were observed. No unmitigated use errors by patients or caregivers were apparent that could result in harm or negative impact on treatment. Based on the safety evaluation, SCTE is well tolerated within the TD patient population.

CONCLUSION

Authentic needle and drug-containing devices were used in order to provide a realistic assessment of the potential for limitations of usability with the SCTE-AI device. Results of this usability validation study indicate the low potential for physical harm associated with use of the device. Results of the study indicate that there is residual risk of (i) not checking the expiration date and (ii) holding the device in place long enough to ensure a complete dose.

The SCTE-AI is intended for use in the at-home setting by the patient or a non-patient caregiver. It may also be used in hospitals, clinics, long-term care and home care settings on adult patients by health care professionals that includes nurses or home health care professionals who may assist patients to use the device in clinical care or home settings. Compared to trained participants, success rates were lower in untrained users who did not read the IFU (reading the IFU improved success rates). From a clinical perspective, these results suggest that it is ideal for each newly prescribed patient to be provided with a first-use in-office specific training on how to use the SCTE-AI. Subsequent to the first-use training, our results suggest a success rate >80% for patients or caregivers with use of the SCTE-AI with minimal use errors.

Overall, the testing in this study is regarded as successful in demonstrating the objective of minimizing the occurrence of preventable use errors. The SCTE-AI device is safe and intuitive to use; is associated with a high rate of injection success, regardless of prior training or experience; and provides patients with an alternative to IM/topical T formulations.

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REFERENCES

1. Morgentaler A, Zitzmann M, Traish AM, et al. Fundamental concepts regarding testosterone deficiency and treatment: International expert consensus resolutions. Mayo Clin Proc 2016;91:881-896.

2. Bhasin S, Brito JP, Cunningham GR, et al. Testosterone therapy in men with hypogonadism: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2018;103:1715-1744.

3. Wu FC, Tajar A, Beynon JM, et al. Identification of late-onset hypogonadism in middle-aged and elderly men. N Engl J Med 2010;363:123-135.

4. Behre HM, Tammela TL, Arver S, et al. A randomized, double-blind, placebo-controlled trial of testosterone gel on body composition and health-related quality-of-life in men with hypogonadal to low-normal levels of serum testosterone and symptoms of androgen deficiency over 6 months with 12 months open-label follow-up. Aging Male 2012;15:198-207.

5. Surampudi PN, Wang C, Swerdloff R. Hypogonadism in the aging male diagnosis, potential benefits, and risks of testosterone replacement therapy. Int J Endocrinol 2012; 2012:625434.

6. Corona G, Isidori AM, Buvat J, et al. Testosterone supplementation and sexual function: A meta-analysis study. J Sex Med 2014;11:1577-1592.

7. Corona G, Giagulli VA, Maseroli E, et al. Testosterone supplementation and body composition: Results from a meta-analysis of observational studies. J Endocrinol Invest 2016; 39:967-981.

8. Snyder PJ, Bhasin S, Cunningham GR, et al. Effects of testosterone treatment in older men. N Engl J Med 2016; 374:611-624.

9. Pfeil E, Dobs AS. Current and future testosterone delivery systems for treatment of the hypogonadal male. Expert Opin Drug Deliv 2008;5:471-481.

10. Smith RP, Khanna A, Coward RM, et al. Factors influencing patient decisions to initiate and discontinue subcutaneous testosterone pellets (Testopel) for treatment of hypogonadism. J Sex Med 2013;10:2326-2333.

11. Kovac JR, Rajanahally S, Smith RP, et al. Patient satisfaction with testosterone replacement therapies: The reasons behind the choices. J Sex Med 2014;11:553-562.

12. Kaminetsky J, Jaffe JS, Swerdloff RS. Pharmacokinetic profile of subcutaneous testosterone enanthate delivered via a novel, prefilled single-use autoinjector: A phase II study. Sex Med 2015;3:269-279.

13. Applying Human Factors and Usability Engineering to Medical Devices Guidance for Industry and Food and Drug Administration Staff. https://www.fda.gov/downloads/MedicalDevices/.../UCM259760.pdf. Accessed March 26, 2018.

14. Wiklund M, Kendler J, Strochlic AY. Usability Testing of Medical Devices. Florida: CRC Press, Taylor & Francis Group; 2016.

15. Yassin A, Almehmadi Y, Saad F, et al. Effects of intermission and resumption of long-term testosterone replacement therapy on body weight and metabolic parameters in hypogonadal in middle-aged and elderly men. Clin Endocrinol (Oxf) 2016; 84:107.

16. AVEED® prescribing information. Malvern, PA: Endo Pharmaceuticals; July 2017. http://www.endo.com/File%20Library/Products/Prescribing%20Information/AVEED_prescribing_information.pdf. Accessed August 2, 2018.

17. Wynia B, Kaminetsky J. Current and emerging testosterone therapies for male hypogonadism. Res Rep Endocr Disord 2015;5:59-69.

18. Rubin J, Chisnell D. Handbook of Usability Testing. 2nd ed. Indiana: Wiley Publishing, Inc; 2008.

SUPPLEMENTARY DATA

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