STS101 (Dry Powder Intranasal Dihydroergotamine) Drug-Device Combination Achieves Consistent and Robust Delivery Performance for Migraine Patients

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Introduction

STS101 (dihydroergotamine nasal powder) is a single dose, drug-device combination product that incorporates proprietary mucoadhesive carrier and engineered drug particle formulation technologies and a proprietary, prefilled, disposable delivery device (Figure 1). STS101 is designed to be intuitive to use (Figure 2) and to provide consistently reliable and robust clinical performance. Features include (i) easy and fast (within seconds) self-administration via a single nostril; and (ii) rapid drug absorption with higher and less variable drug plasma levels achieved more quickly as compared with DHE nasal liquid formulation products. The STS101 design overcomes many of the limitations of DHE nasal liquid formulation products, including difficulty in correctly self-administering arising from the need for assembly, priming, and administration of multiple liquid sprays into both nostrils at intervals up to 15 minutes apart to achieve a full dose; nasal drip-out and run-off to pharynx; and low, slow, and highly variable pharmacokinetics (PK) which may result in poor and/or inconsistent clinical performance.

The PK, safety, and tolerability of STS101 in a Phase I trial were previously reported (see Figure 3 and poster IHC2019-597), and STS101 is currently being evaluated in a large, randomized double-blind, placebo-controlled efficacy trial (Phase III EMERGE study; refer to NCT03901482).

Objective

To determine if intra- or inter-patient variability in actuating ("squeezing") the STS101 pump to self-administer drug could result in variability in the amount of drug delivered by the STS101 nasal delivery device, we evaluated and here report the amounts of DHE delivered under variable pump squeezing conditions. In addition, to determine potential for lung exposure to the STS101 formulation following nasal administration (and thereby confirm that pulmonary safety risk is minimal) we evaluated and here report that the potentially respirable fine particle mass (i.e., the mass of particles with aerodynamic particle size (APS) <5 µm) associated with administration of STS101 is less than the target threshold of 5% of delivered dose.

Methods

Dose testing was performed with a computer-controlled auto-actuator (Proveris Vereo DSx), in which the squeeze velocity and displacement (full or partial squeeze) of the device pump was varied to simulate a range of patient use conditions. APS distribution (APSD) testing was performed with a cascade impactor (Next Generation Impactor (NGI)) to determine the fraction of potentially respirable fine particles less than 5 µm in the delivered dose. APSD testing is a well-validated means of assessing how much drug may potentially be delivered to the lungs.

Results

- Varying device squeezing parameters resulted in delivery of 96% mean dose with 3.5% relative standard deviation demonstrating that STS101 robustly and consistently delivers DHE dose irrespective of variability in squeezing (Figures 4 and 5).
- >95% of the target amount was delivered even when lowering the squeeze speed to 50% of the normal value (Figure 4).
- 1.3% of the delivered dose had particles with APS <5 µm, demonstrating very low potential for lung deposition and supporting pulmonary safety of STS101 (Figure 6).

Discussion / Conclusion

- STS101 demonstrates robust and consistent delivery even when varying the squeezing parameters of the device pump.
- STS101 consistently delivers the full dose and has optimal APSD for nasal deposition with negligible respirable fine particle mass (i.e., very low lung deposition).
- STS101 has the delivery characteristics to satisfy the unmet need for a reliable non-parenteral form of DHE.

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STS101 (Dihydroergotamine Nasal Powder)

Figure 1. STS101

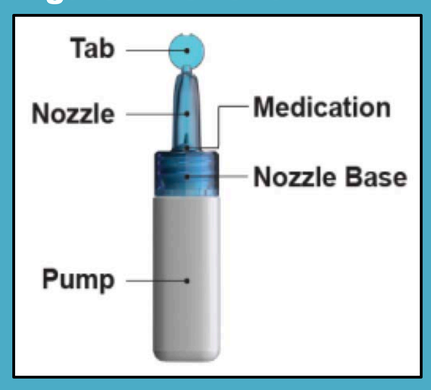


Figure 2. STS101 Use

- Self-administered, single-use, disposable drug-device combination product for acute treatment of migraine
- Designed for rapid, convenient, and intuitive self-administration with no assembly or priming required
- Delivered dose is highly reproducible and insensitive to varied actuation ("squeezing") conditions
- Low PK variability demonstrated in Phase I PK trial

Figure 3. Phase I Human PK Data

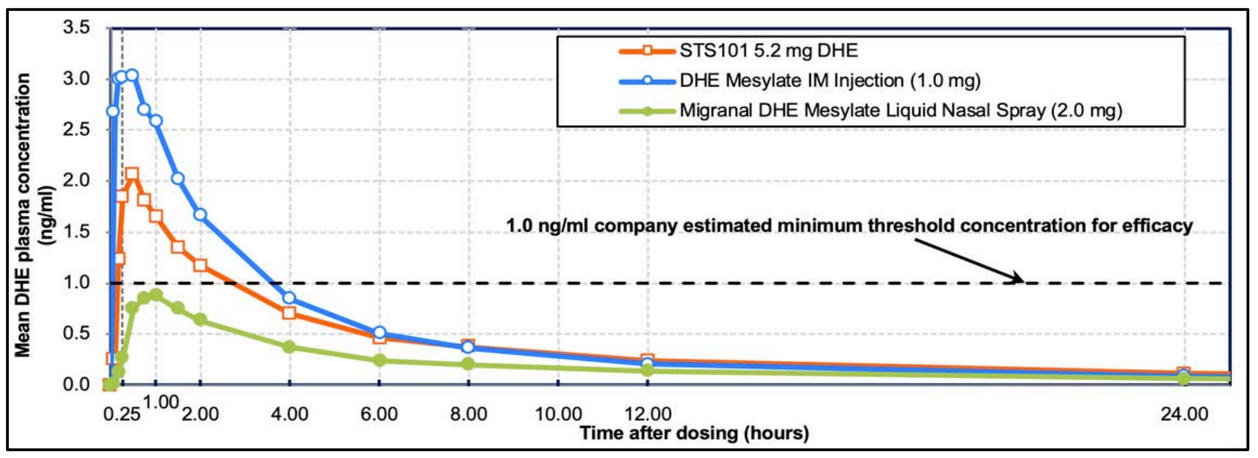
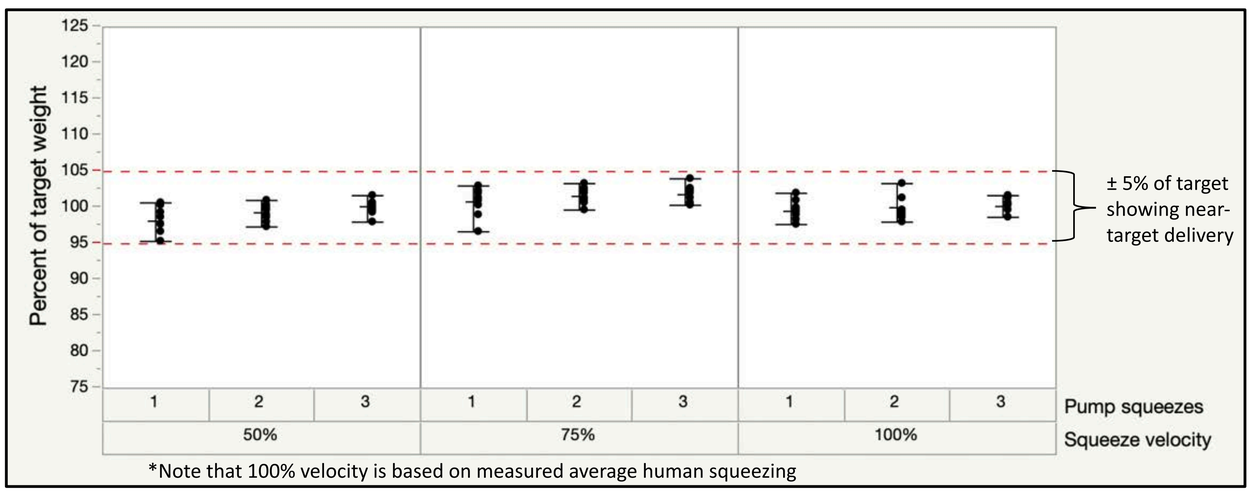


Figure 4. STS101 Consistently Achieves Target Delivery Irrespective of the Number of Squeezes and Squeeze Velocity



*Note that 100% velocity is based on measured average human squeezing

Figure 5. STS101 Consistently Achieves Target Delivery when Varying Squeeze Velocity and Squeeze Displacement (Full or Partial)

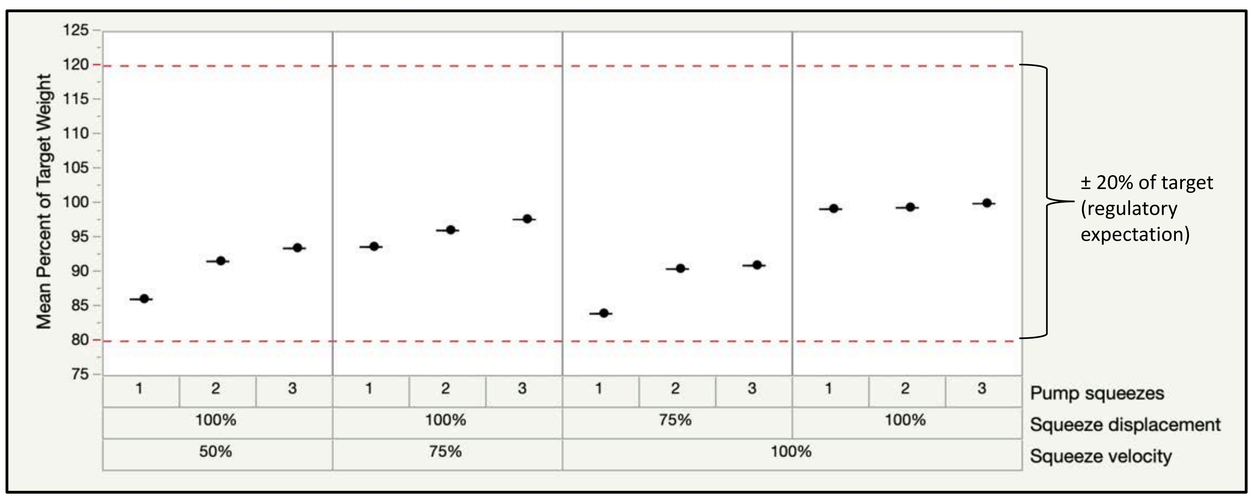


Figure 6. STS101 Demonstrates Very Low Potentially Respirable Fraction as Shown by APSD Testing Using NGI