Efficacy and Safety of STS101 DHE Nasal Powder for the Acute Treatment of Migraine: Results from the Phase 3 Double-Blind, Randomized, Placebo-Controlled SUMMIT Study

Richard B. Lipton, MD[1]; Stewart Tepper, MD[2]; Detlef Albrecht, MD[3]

[1]Albert Einstein College of Medicine/Montefiore Medical Center, [2]Geisel School of Medicine at Dartmouth, [3]Satsuma Pharmaceuticals, Inc.

Introduction

- Dihydroergotamine mesylate (DHE) is a recommended first-line option for the acute treatment of moderate or severe migraine attacks with or without aura.[1]
- STS101 is a novel investigational DHE product that combines a mucoadhesive nasal powder formulation with an easy-to-use, easy-to-carry, pre-filled, single-use nasal delivery device.
- The STS101 advanced nasal powder and device technology maximizes deposition of DHE on the nasal mucosa, enhancing DHE absorption, increasing drug exposure and reducing pharmacokinetic variability in comparison with DHE liquid nasal sprays.
- STS101 is the only DHE-containing product with double-blind, placebo-controlled Phase 3 data using modern migraine clinical trial endpoints recommended by the FDA and the International Headache Society. [2,3]

Objective

To compare the efficacy and safety of STS101 5.2 mg, a novel investigational DHE nasal powder, with placebo in the acute treatment of migraine with or without aura in a double-blind, randomized, placebo-controlled Phase 3 study (SUMMIT).

Methods

Study design and treatment intervention

- SUMMIT (NCT04940390) was a double-blind, randomized, placebo-controlled Phase 3 trial in adults with a history of 2-8 moderate or severe migraine attacks and fewer than 15 headache days per month.
- After establishing eligibility, a subject self-administered a single dose of STS101 5.2 mg or placebo to treat one migraine attack of moderate or severe pain intensity.

Subjects

- Study subjects must have had ≥1-year history of migraine with or without aura according to the ICHD-3 criteria,[4] including:
  - Migraine onset before the age of 50
  - 2–8 migraine attacks/month with moderate or severe pain each month
  - <15 headache days/month
- Subjects with a non-migraine headache diagnosis, history of cerebrovascular disease, ≥1 cardiovascular risk factors, and use of >1 migraine preventative were excluded.

Outcomes and analyses

- Pain was assessed from 15 minutes through 48 hours after study treatment on a 4-point scale where 0 is no pain and 3 is severe pain.
  - Pain freedom (PF) was defined as a reduction of moderate or severe headache pain (2 or 3 on the scale) to no headache pain (0 on the scale) with no prior use of any rescue medication.
  - Pain relief (PR) was defined as a reduction of moderate or severe headache pain (2 or 3 on the scale) to mild or no headache pain (1 or 0 on the scale) with no prior use of any rescue medication.
- The co-primary efficacy endpoints were PF and MBSF at 2 hours post-dose. Secondary endpoints included PF, MBSF, and PR over 48 hours post-dose.
- MBS freedom (MBSF) was defined as the absence of the self-identified MBS (i.e., photophobia, phonophobia, or nausea) with no prior use of any rescue medication and was also assessed from 15 minutes through 48 hours after study treatment
- For timepoints with missing data, a last-observation-carried-forward imputation was used.
- Treatment-emergent adverse events (TEAEs) are summarized descriptively for the all-subjects safety population (i.e., all subjects used study medication).

Results

Subjects

- Of 1591 randomized subjects, 1424 (mean age 39 years, 79% female) were evaluable for efficacy (STS101, n=716; placebo, n=708) (Figure 2).
- The treated attacks showed high rates of severe pain (38%), nausea (69%), photophobia (96%), phonophobia (91%), and allodynia (63%) (Table 1).

PF and MBSF Through 48 Hours Post-Dose

- STS101 demonstrated numerical, but not statistically significant superiority over placebo on PF and MBSF at the pre-specified 2-hour co-primary endpoints (Figure 3).
- Highly significant (p<0.001) improvements in PF and MBSF were achieved by 3 hours through 48 hours post-dose (Figure 3).

PR Through 48 Hours Post-Dose

- STS101 significantly improved PR at 2 hours through 48 hours post-dose (Figure 4).

Treatment-Emergent Adverse Events

- The most common (≥2%) TEAE (STS101 versus placebo) were nasal discomfort (8.3% versus 1.5%) and dysgeusia (3.7% versus 0.3%). Most TEAEs were mild, and none were serious (Table 2).

Figure 1. STS101 Administration

Figure 2. Subject Disposition

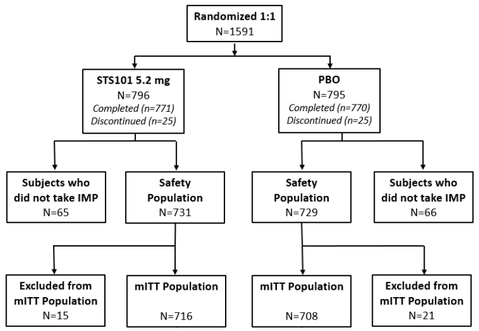


Table 1. Subject Demographics

Variable	5.2 mg STS101 (n=716)	Placebo (n=708)
Age (mean; SD)	38.2 (11.4)	38.9 (11.5)
Gender (% M/F)	21/79	20/80
Race (%)		
White	82.5	81.4
African American	12	13.7
Asian	3.5	3.4
Other	2.0	1.5
Years since onset (mean; SD)	16.2 (11.3)	16.9 (11.4)
Monthly reported before screening:		
# of moderate/severe migraines (SD)	4.5 (1.7)	4.5 (1.7)
# of headache days (SD)	6.9 (2.7)	6.9 (3.0)
Subjects on prevention medication at randomization (%)	10.2	10.2
HIT-6 (mean; % >60=severe impact)	64.2 (88.1)	64.1 (86.4)

Figure 3. PF and MBSF Through 48 Hours Post-Dose

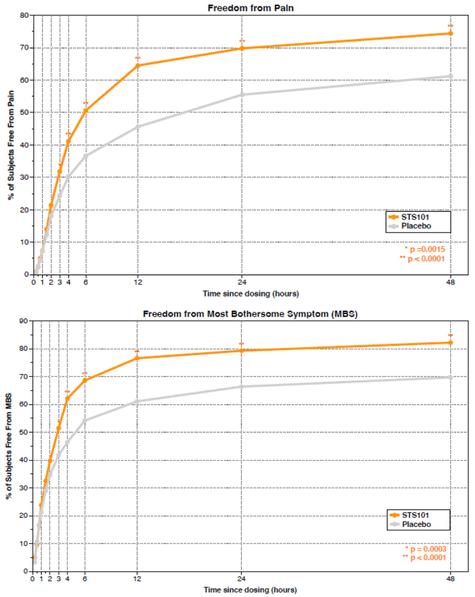
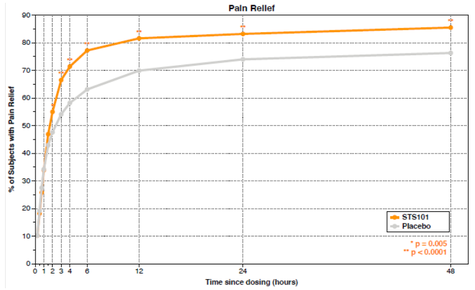


Figure 4. PR Through 48 Hours Post-Dose



Conclusions

- Single-dose STS101 DHE nasal powder did not achieve efficacy at the co-primary 2-hour endpoints versus placebo.
- Single-dose STS101 DHE nasal powder showed significant anti-migraine effects on pain freedom (3-48 hours post-dose), freedom from most bothersome symptom (3-48 hours post-dose), and pain relief (2-48 hours post-dose).
- STS101 showed a favorable safety and tolerability profile.

Disclosures

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