# Efficacy of STS101 DHE Nasal Powder for the Acute Treatment of Difficult to Treat Migraines: Results from the Phase 3 Double-Blind, Randomized, Placebo-Controlled SUMMIT Study

Jessica Ailani, MD[1]; Detlef Albrecht, MD[2]; and Robert Cowan, MD[3]

[1]Georgetown University, [2]Satsuma Pharmaceuticals, Inc., [3]Stanford University

## 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 power formulation with an easy-to-use, easy-to-carry, pre-filled, single-use nasal delivery device (Figure 1).
- 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 of STS101 5.2 mg, a novel investigational DHE nasal powder, with placebo in the acute treatment of migraine attacks with nausea, allodynia, and during menstruation in the 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.
- 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.
- If the subject treated a migraine attack within 1 (± 2) days of menstruation, then the subject was considered as having a menstruation related acute migraine attack.
- Allodynia status was defined as present if a subject had a least 2 "yes" responses to the 6-question allodynia questionnaire.[5,6]
- Subjects who did not have evaluable assessments at the 2-hour timepoint, or who received rescue medications prior to the 2-hour tie point were considered non-responders.[7]

## Results

### Subjects

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

### Migraine Attacks with Allodynia at Baseline

- STS101 demonstrated statistically significant superiority over placebo on PF and MBSF from 4 through 24 hours post-dose (Figure 2).

### Migraine Attacks with Nausea at Baseline

- STS101 demonstrated statistically significant superiority over placebo on PF and MBSF from 3 hours through 48 hours post-dose (Figure 3).

### Migraine Attacks in Menstrually Related Migraine Attacks

- STS101 demonstrated statistically significant superiority over placebo on PF from 4 through 12 hours post-dose and MBSF from 4-6 and 48 hours (Figure 4).

**Figure 1. STS101 Administration**


**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 2. PF and MBSF in Migraine Attacks with Allodynia at Baseline**

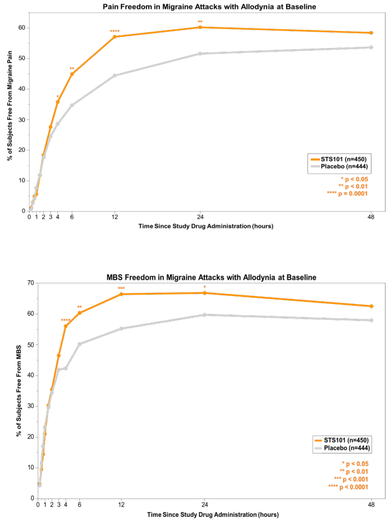



**Figure 3. PF and MBSF in Migraine Attacks with Nausea at Baseline**

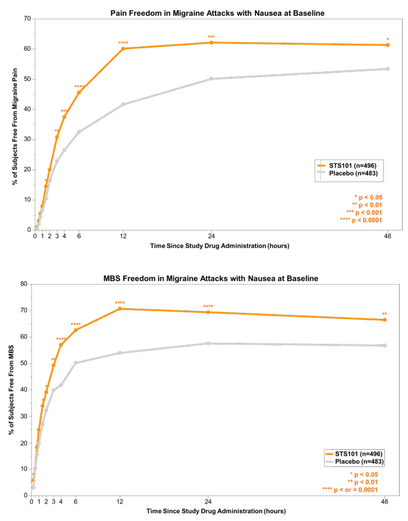
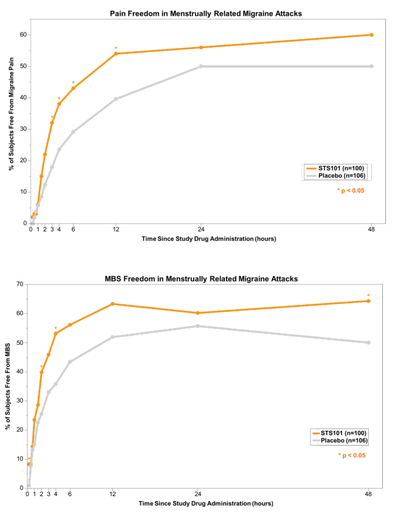



**Figure 4. PF and MBSF in Menstrually Related Migraine Attacks**




## Conclusions

- Single-dose STS101 DHE nasal powder was effective in providing freedom from migraine pain and most bothersome symptom in difficult to treat migraine attacks including migraine attacks with allodynia at baseline and migraine attacks with nausea at baseline.
- STS101 showed improvement in freedom from migraine pain from 3 through 12 hours and most bothersome symptom at 4 hours in subjects with menstrually related migraine, but the limited number of events may have impacted the significance of other timepoints.

### Disclosures

*Dr. Ailani is* an advisor for Abbvie, Amgen, Aeon, Axsome, Biohaven, BioDeliveryScientificInternational, Eli Lilly, GlaxosmithKline, Lundbeck, Linpharma, Impel, Miravio, Pfizer, Neurolief, Satsuma, Theranica, and Teva; holds clinical trial grants from Abbvie, Biohaven, Eli Lily, Satsuma, and Zosano; has stock options in ClrtM, and is on the Editorial Boards or Steering Committee for Medscape, NeurologyLive, Current Pain and Headache, and SELF magazine.

*Dr. Cowan* is an advisor for Teva, Allergan/Abbvie, Lundbeck, Amgen, Theranica, Rehaler, Biohave/Pfizer, and Satsuma; has royalties for Springer, Penguin/Avery, and Oxford; is Principle in BonTriage, Inc.; and has equity/options in AgoneX, 30 Madison, and Percept.

*Dr. Albrecht* was an employee and stockholder of Satsuma Pharmaceuticals at the time of study conduct and is now a consultant for and stockholder for Satsuma Pharmaceuticals.

### Acknowledgements

This study and publication were funded by Satsuma Pharmaceuticals (South San Francisco, CA) in accordance with Good Publication Practice guidelines.

### References

1. Ailani J, et al. *Headache*. 2021;61(7):1021-1039.
2. FDA Acute Migraine Guidance, 2018.
3. Diener H-C, et al. *Cephalalgia*. 2019;39(6):687-710.
4. Headache Classification Committee of the International Headache Society (IHS). *Cephalalgia*. 2018;38(1):1-211.
5. Ashkenazi A, et al. *Cephalalgia*. 2007:27(2):111-7.
6. Tepper, S. et al. *Headache*. 2012;52:37-47.
7. Study STS101-007 clinical study report statistical analysis plan.