P-693

Long-Term Safety and Tolerability Data of STS101 From the Phase 3 Open-Label ASCEND Study

Stewart J. Tepper, MD[1], Amaal J. Starling, MD[2], Shannon Strom, PhD[3], Detlef Albrecht, MD[3]

[1]New England Institute for Neurology and Headache, Stamford, CT, USA; [2]Mayo Clinic, Scottsdale, AZ, USA; [3]Satsuma Pharmaceuticals, Inc., Durham, NC, USA

Introduction

- Dihydroergotamine mesylate (DHE) is a recommended first-line treatment 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 delivered 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.[2]

Objective

- The ASCEND study assessed the safety and tolerability of STS101 5.2 mg in the acute treatment of migraine attacks with or without aura over 12 months.

Methods

Study Design and Treatment Intervention

- ASCEND was a multi-center, multi-dose, open-label, 12-month study of STS101 in adults aged 18–65 years with migraine (NCT04406649).
- After establishing eligibility, the participants could self-administer STS101 5.2 mg for up to 2 doses within 24 hours to treat a single migraine attack, and up to 12 doses/month for 12 months.

Participants

- Study participants must have had ≥1-year history of migraine (with or without aura) according to the International Classification of Headache Disorders, 3rd edition, including[3]:
  - Migraine onset before age of 50 years
  - 4–12 migraine attacks/month in each of the 3 months prior to screening
  - <15 headache days/month in each of the 3 months prior to screening
- Exclusion criteria included diagnosis of non-migraine headache, history of cerebrovascular disease, and ≥2 cardiovascular risk factors.
- Participants must have an intact nasal mucosa at baseline (i.e., no ulceration or bleeding; no or mild erythema, swelling, and rhinorrhea).

Outcomes and Analyses

- Safety evaluations included physical and nasal examinations, vital signs, ECGs, laboratory tests, and treatment emergent adverse event (TEAE) assessments.
- TEAE assessments were performed at every study visit (months 1–6, 8, 10, and 12).
- Nasal safety assessments included nasal examinations with standardized assessments of nasal findings, subjective assessments of nasal irritation, smell identification test (SIT), and recording of TEAEs related to nasal/administration.
- Objective nasal assessments were done by trained study personnel on a 4-point severity scale (0=none, 1=mild, 2=moderate, and 3=severe) to document nasal erythema, edema, rhinorrhea, bleeding, and nasal mucosa ulcerations.
- This safety analysis included those participants who exclusively used the nasal delivery device planned for commercialization.

Results

- The safety population included 344 participants who treated 6,610 migraine attacks with a total of 8,234 doses of STS101.
  - Mean ± SD age: 40 ± 11 years
  - 86% female
  - 87.5% Caucasian (44% Hispanic)
- Of the total migraine attacks, 1,315 (19.9%) were treated with a second dose of STS101.
- In total, 167 (48.5%) participants experienced TEAEs across 1,216 (18.4%) migraine attacks, with the most frequent being nasal discomfort (11.3%), dysgeusia (7.6%), and nasal congestion (5.2%) (Table 1).
- Treatment-related TEAEs were observed in 11.8% of migraine attacks (n=777/6,610).
- TEAEs were generally mild and transient, with no treatment-related SAEs.
- A total of 15 (4.4%) participants discontinued the study due to TEAEs, which were deemed treatment-related (Table 2).
- One serious TEAE (NSTEMI) was reported in a participant that should have been excluded from the study due to prior myocardial infarction and other conditions disqualifying for study participation.
- Local TEAEs occurred at similar rates between the 1,315 attacks treated by participants who administered a second STS101 dose to treat ≥1 attack relative to the 5,295 migraine attacks treated by participants who only used a single dose for treatment (Table 3).
- No clinically relevant changes in physical exams, vital signs, nasal examinations, subjective nasal irritation assessments, electrocardiograms, lab test, or SIT were observed.

Figure 1. STS101 Administration

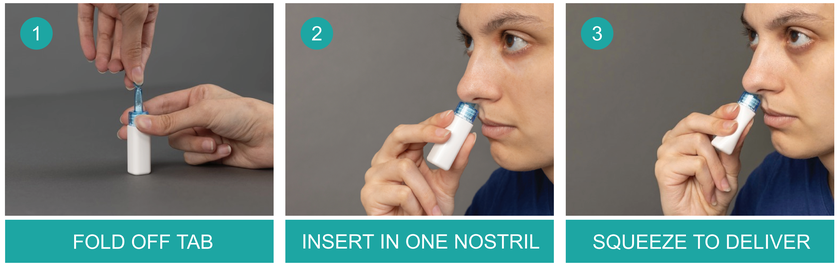

Table 1. Summary of Reported TEAEs

	By participant N=344	By attack N=6,610
	n (%) with ≥1 TEAE	n (%) with ≥1 TEAE
Any TEAE, n (%)	167 (48.5)	945 (14.3)
Severe	9 (2.6)	13 (0.2)
Moderate	81 (23.5)	142 (2.1)
Mild	133 (38.7)	844 (12.8)
Local TEAE, n (%)	99 (28.8)	769 (11.6)
Treatment-related TEAE, n (%)	89 (25.9)	777 (11.8)
Most frequent treatment-related TEAE	**n (%) reporting TEAE at least once**	**n (%) attacks with TEAE**
Nasal discomfort	39 (11.3)	425 (6.4)
Dysgeusia (abnormal taste sensation)	26 (7.6)	196 (3.0)
Nasal congestion	18 (5.2)	253 (3.8)
Nasopharyngitis	18 (5.2)	20 (0.3)

TEAE, treatment-emergent adverse event.

Table 2. Treatment Discontinuations Due to TEAEs

	By participant N=344
Any TEAE leading to discontinuation, n (%)	15 (4.4%)
Rhinalgia	3 (0.9)
Nasal discomfort	2 (0.6)
Epistaxis (nosebleed)	1 (0.3)
Sneezing	1 (0.3)
Throat tightness	1 (0.3)
Vomiting	1 (0.3)
Dysgeusia (abnormal taste sensation)	1 (0.3)
Rhinitis	1 (0.3)

TEAE, treatment-emergent adverse event.

Table 3. Summary of Local TEAEs Reported by ≥2% of Participants in Attacks Treated With 1 or 2 Doses of STS101

	2 doses of STS101 used to treat ≥1 migraine attack		1 dose of STS101 used to treat ≥1 migraine attack	
	By participant N=185	By attack N=1,315	By participant N=159	By attack N=5,295
Any TEAE, n (%)	53 (28.6)	207 (15.7)	46 (28.9)	703 (13.3)
Nasal discomfort	23 (12.4)	78 (5.9)	16 (10.1)	347 (6.6)
Dysgeusia (abnormal taste sensation)	6 (3.8)	32 (2.4)	20 (10.8)	164 (3.1)
Nasal congestion	12 (6.5)	43 (3.3)	6 (3.8)	210 (4.0)
Nasopharyngitis	4 (2.2)	3 (0.2)	14 (8.8)	17 (0.3)
Rhinorrhea (runny nose)	11 (5.9)	11 (0.8)	4 (2.5)	65 (1.2)
Rhinalgia (pain in nose)	7 (3.8)	11 (0.8)	3 (1.9)	37 (0.7)
Epistaxis (nosebleed)	4 (2.2)	5 (0.4)	4 (2.5)	5 (<0.1)

TEAE, treatment-emergent adverse event.

Conclusions

- The results of the ASCEND study show that STS101 was well tolerated when used long-term and as needed by participants with migraine.
- TEAEs were mostly local, mild, and transient.
- Incidence of discontinuations due to TEAEs was low.
- Nasal evaluations, ECGs, and blood pressure assessments showed no clinically relevant changes.
- The use of a second STS101 dose for the same attack did not lead to an increase in TEAEs.

References

1. Ailani J, et al. *Headache*. 2021;61(7):1021-1039.
2. Lipton R, et al. *Headache*. 2024;64(3):266-75.
3. ICHD-3. *Cephalalgia*. 2018;38(1):1-211.

Disclosures

Dr. Tepper received research grants (no personal compensation) from Allergan/Abbvie, Amgen, Eli Lilly, Lundbeck, Neurolief, Novartis, Satsuma, Zosano; is a consultant and/or advisory board member (honoraria) for Aeon, Allergan/Abbvie, Alphasights, Amgen, Aruene, Atheneum, Axsome Therapeutics, Becker Pharmaceutical Consulting, BioDelivery Sciences International, Biohaven, ClearView Healthcare Partners, CoolTech, CRG, Curvia, Decision Resources, Defined Health, DRG, Eli Lilly, ExpertConnect, FCB Health, Fenix, GLG, Guidepoint Global, Health Advances, Health Science Communications, HMP Communications, Impel, InteractiveForums, Keyquest, King and Partners, Lundbeck, MJ Global Research, Satsuma, Teva, and Theranica; Magnolia Innovation, MJH Holdings, Neurolief, Novartis, P Value Communications, Pain Insights, Inc, Palion Medical, Pulmatrix, Putnam Associates, SAI MedPartners, Satsuma, Slingshot Insights, Spherix Global Insights, Strategy Inc, System Analytic, Taylor and Francis, Teva, Theranica, Tremeau, Trinity Partners, Unity HA, XOC, Zosano; receives salary from Dartmouth-Hitchcock Medical Center, Thomas Jefferson University; received CME honoraria from American Academy of Neurology, American Headache Society, Annenberg Center for Health Sciences, Catamount Medical Education, Diamond Headache Clinic, Forefront Collaborative, Haymarket Medical Education, Medical Education Speakers Network, Medical Learning Institute Peerview, Migraine Association of Ireland, Miller Medical Education, National Association for Continuing Education, North American Center for CME, The Ohio State University, Physicians' Education Resource, PlatformQ Education, Primed, Texas Neurological Society, Vindico Medical Education, WebMD/Medscape.

Dr. Starling has received consulting fees from Allergan, Amgen, Axsome Therapeutics, Eli Lilly, Everyday Health, Impel, Lundbeck, Med-IQ, Medscape, Neurolief, Novartis, Satsuma, Teva, and Theranica.

Dr. Strom is an employee of Satsuma Pharmaceuticals and was a stockholder at the time of study conduct.

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 (Durham, NC). The authors thank The Medicine Group, LLC (New Hope, PA, USA) for providing medical writing support, which was funded by Satsuma Pharmaceuticals, Inc. and in accordance with Good Publication Practice guidelines.

Presented at the American Headache Society (AHS) Annual Meeting; June 13–16, 2024