STS101 (Dihydroergotamine Nasal Powder) Shows Benefit on the Resolution of Cardinal Migraine Symptoms Photophobia, Phonophobia, and Nausea: Results From the Long-Term Phase 3 Open-Label ASCEND Study

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Introduction

- Dihydroergotamine (DHE) mesylate is a recommended first-line treatment option for the acute treatment of moderate or severe migraine attacks, with or without aura.[1]
- STS101 (ATZUMI™) is an FDA-approved drug-device combination of a DHE mesylate powder formulation prefilled in a single-use delivery device for nasal administration.[2]
- 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

- To evaluate the cardinal symptom (nausea, photophobia, and phonophobia) reduction capabilities of STS101 in the acute treatment of migraine from the ASCEND study

Methods

Study Design and Treatment Intervention

- ASCEND was a multicenter, 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 as needed for up to 2 doses within 24 hours to treat a single migraine attack, and up to 12 doses/month for 12 months.
- As an open-label study, all effectiveness analyses were exploratory.

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,[3] including:
  - 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.

Outcomes and Analyses

- Efficacy data are presented for migraines in the modified intent-to-treat (mITT) population, defined as all participants who treated ≥1 migraine attack with study medication from the final version of STS101 and had ≥1 post-baseline efficacy data reported in an eDiary.
- The cardinal symptoms of nausea, photophobia, and phonophobia were assessed at baseline immediately before treatment of the migraine headache and up to 48 hours after treatment.
  - Freedom from nausea, photophobia, or phonophobia was defined as an absence of nausea, photophobia, or phonophobia post-dose if present at baseline.

Results

- Of the 344 adults enrolled, 335 used the final device to treat 6610 migraine attacks (Table 1).
- The treated attacks identified high rates of nausea (60%), photophobia (94%), and phonophobia (92%) at baseline (Table 2).
- In the attacks with photophobia at baseline, over half were free from photophobia by 2 hours post-dose and about 92% by 24 hours, respectively (Table 2, Figure 1).
- In the attacks with phonophobia at baseline, about one third were free from phonophobia by 1 hour post-dose and about 94% by 24 hours, respectively (Table 2, Figure 2).
- In the attacks with nausea at baseline, almost half were free from nausea by 1 hour post-dose and about 95% by 24 hours, respectively (Table 2, Figure 3).
- Over 90% of the attacks were free from all cardinal symptoms by 24 hours.
- Similar symptom resolution rates were reported when the specific symptom was selected as the most bothersome symptom.

Table 1. Baseline Demographics and Characteristics

	STS101 5.2 mg N=344
Mean (SD) age, years	40.4 (10.9)
Sex, n (%)	
Male	49 (14.2)
Female	295 (85.8)
Ethnicity, n (%)	
Hispanic or Latino	150 (43.6)
Not Hispanic or Latino	194 (56.4)
Race, n (%)	
White	301 (87.5)
Black or African American	32 (9.3)
Asian	8 (2.3)
Other	3 (0.9)
Years since onset, mean (SD)	18.5 (11.6)
Monthly migraines reported before screening, mean (SD)	5.5 (1.6)*
Monthly headache days reported before screening, mean (SD)	7.5 (2.9)*
Allodynia: yes, n (%)	109 (31.7)
Aura: yes, n (%)	163 (47.4)
Nausea: yes, n (%)	291 (84.6)
Photophobia: yes, n (%)	335 (97.4)
Phonophobia: yes, n (%)	327 (95.1)

*n=170.

Table 2. Proportion of Attacks With Freedom From Cardinal Symptoms Over 48 Hours Post-Dose

	Photophobia (%)	Phonophobia (%)	Nausea (%)
1 Hour	26.5	32.6	48.5
2 Hours	52.9	58.3	69.7
4 Hours	77.7	80.3	87.5
24 Hours	91.6	93.8	94.5
48 Hours	94.1	94.7	93.9

Figure 1. Proportion of Attacks With Freedom From Photophobia Through 48 Hours Post-Dose

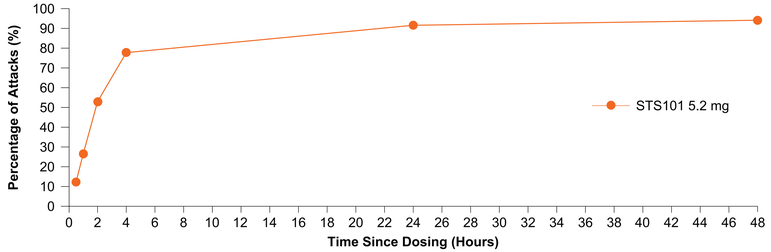


Figure 2. Proportion of Attacks With Freedom From Phonophobia Through 48 Hours Post-Dose

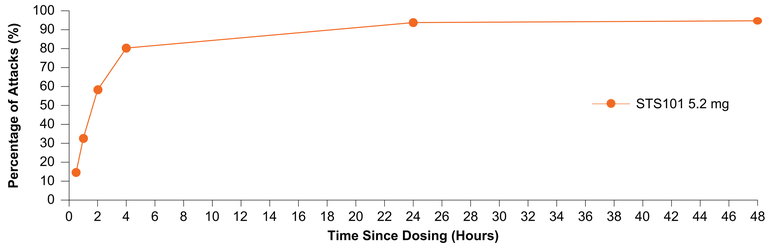
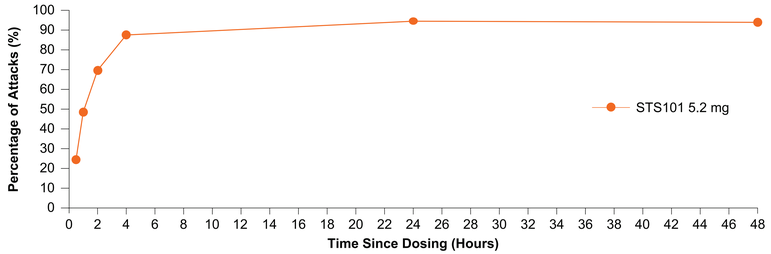


Figure 3. Proportion of Attacks With Freedom From Nausea Through 48 Hours Post-Dose



Conclusions

- The results of the ASCEND study show that, similar to its effects on migraine headache pain and most bothersome headache-associated symptom, STS101 demonstrated rapid and sustained resolution of each of the cardinal migraine symptoms of photophobia, phonophobia, and nausea.
- Specifically, the effect on nausea is noteworthy as other routes of DHE administration have been related to an increase in nausea.

References

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Disclosures

Dr. Starling has received consulting fees from AbbVie, Allergan, Amgen, Amneal, Axsome Therapeutics, Eli Lilly, eNeura, Everyday Health, Impel, Lundbeck, Med-IQ, Medscape, Miller Medical, Neurolief, Novartis, Pfizer, Salvia, Satsuma, Teva, Theranica, and WebMD.
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Dr. Strom 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.
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