MORNING AND EVENING NASAL SYMPTOM IMPROVEMENT WITH OLOPATADINE/MOMETASONE COMBINATION NASAL SPRAY IN PATIENTS WITH SEASONAL ALLERGIC RHINITIS

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ABSTRACT

Statement of Purpose

In two phase 3, randomized, double-blind seasonal allergic rhinitis (SAR) studies, twice-daily GSP301 nasal spray—an investigational fixed-dose combination of olopatadine hydrochloride (HCl) and mometasone furoate—significantly improved the combined average morning (AM) and evening (PM) 12-hour reflective Total Nasal Symptom Scores (rTNSS) versus placebo (primary endpoint, presented elsewhere), as well as the average AM/PM instantaneous TNSS (iTNSS) versus placebo (secondary endpoint, presented elsewhere). Results of additional endpoints—separate analysis of the AM and PM nasal symptoms comparing GSP301 versus placebo—are reported here.

Statement of Methods

In Study 1 (NCT02631551; N=1,180) and Study 2 (NCT02870205; N=1,176), patients ≥12 years of age with SAR were randomized 1:1:1:1 to GSP301 (olopatadine HCl 665 µg/mometasone furoate 25 µg), olopatadine HCl (665 µg), mometasone furoate (25 µg), or placebo twice-daily for 14 days. Least squares mean differences (LSMD) from baseline to end of treatment in average AM and average PM rTNSS, iTNSS and individual nasal symptoms (nasal congestion, rhinorrhea, nasal itching, and sneezing) and LSMD on each treatment day for average AM and PM TNSS for GSP301 versus placebo were separately analyzed using mixed-effect model repeated measures, adjusting for covariates (P<0.05=statistically significant).

Summary of Results

When analyzed separately, GSP301 treatment resulted in statistically significant improvements versus placebo on the average AM and the average PM rTNSS in both studies (P<0.001, all). Similar significant improvements were observed for average AM iTNSS and average PM iTNSS in both studies (P<0.001; all). Importantly, GSP301 significantly improved each AM and each PM individual nasal symptom for rTNSS and iTNSS versus placebo in both studies (P<0.05, all). Further, GSP301 improved AM and PM rTNSS and iTNSS on each of the 14 treatment days in both studies versus placebo. Improvements were significant on both the AM and PM rTNSS and iTNSS on days 1-14 in Study 2 (P≤0.001, all). In Study 1, GSP301 significantly improved AM rTNSS, AM iTNSS, and PM iTNSS on each treatment day (P≤0.01, all). GSP301 also provided significant improvements in PM rTNSS on days 2-14 (P≤0.001, all), with improvements on day 1 approaching statistical significance (P=0.073).

Conclusion

When AM and PM nasal symptoms were analyzed separately in 2 replicate SAR studies, GSP301 resulted in greater improvements versus placebo for both the average AM and the average PM nasal symptoms. Importantly, the significant nasal symptom improvements seen with GSP301 versus placebo in the pre-dose AM and pre-dose PM iTNSS indicate that efficacy was maintained over the entire 12-hour twice-daily dosing interval throughout the 14-day treatment period.

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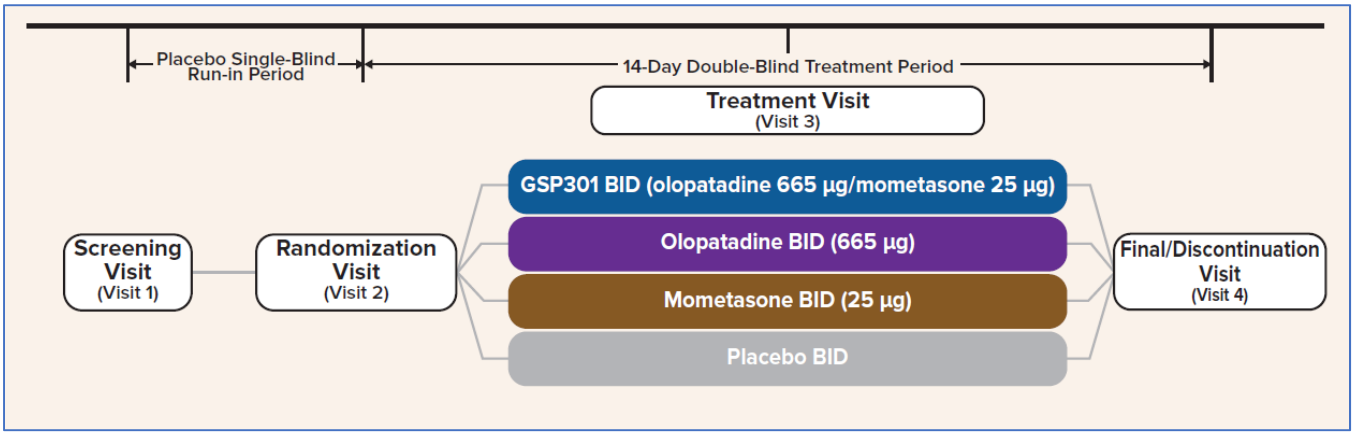
KEY FINDINGS

STUDY DESIGN

- Two similarly designed double-blind, randomized, parallel-group studies were conducted during the spring (Study 1, NCT02631551) and fall/mountain cedar (Study 2, NCT02870205) pollen seasons in patients with SAR (**Figure 1**)
- Twice daily, patients self-administered study medication and self-assessed AM and PM reflective and instantaneous nasal symptoms (nasal congestion, rhinorrhea, itchy nose, and sneezing) and ocular symptoms (itching/burning, tearing/watering, and redness of eyes) in a symptom diary

Figure 1. Study Design



GSP301, olopatadine 665 µg/mometasone 25 µg BID; olopatadine, 665 µg BID; mometasone, 25 µg BID.
Studies 1 and 2 were of similar design except for the allergy season during which each was conducted: Study 1 was conducted during the spring allergy season and Study 2 during the fall/mountain cedar allergy season. The screening visit (visit 1) occurred between day -10 and day -7 prior to the randomization visit on day 1 (visit 2). The treatment visit (visit 3) occurred on approximately day 8, and the final/discontinuation visit (visit 4) occurred on approximately day 15. Only results pertaining to GSP301 versus placebo are reported here.
BID, twice-daily.

Endpoints

- Endpoints were mean change from baseline to end of 14-day treatment in:
  - Average AM rTNSS and iTNSS
  - Average PM rTNSS and iTNSS
  - Average AM individual nasal symptoms (rTNSS and iTNSS)
  - Average PM individual nasal symptoms (rTNSS and iTNSS)
- Additional endpoints included mean change from baseline by day in:
  - Average AM rTNSS and iTNSS
  - Average PM rTNSS and iTNSS
- Only results pertaining to GSP301 and placebo are reported here
- The primary efficacy endpoint—mean change from baseline to the end of treatment in patient-reported AM and PM 12-hour rTNSS over the 14-day treatment period—and safety results for both trials have been reported elsewhere[1,2]

KEY FINDINGS

RESULTS

Patients

- A total of 1,180 and 1,176 patients were randomized in Studies 1 and 2, respectively
- Demographics and baseline symptom scores were similar across the treatment groups:
  - Patients were predominantly female, white, and non-Hispanic/Latino, with mean ages ranging from 39.4 to 39.9 years
  - Average baseline AM and average PM rTNSS scores ranged from 10.1 to 10.4, and average AM and average PM iTNSS scores ranged from 9.3 to 9.6

Efficacy

- When analyzed separately, GSP301 treatment resulted in statistically significant improvements versus placebo on the average AM and the average PM rTNSS in both studies (P<0.001, all; **Table 1)**
- Similar significant improvements were observed for average AM and average PM iTNSS in Studies 1 and 2 (P<0.001; all; **Table 1**)
- Importantly, GSP301 significantly improved each average AM and each average PM individual nasal symptom (nasal congestion, itching, rhinorrhea, sneezing) for rTNSS and iTNSS versus placebo in both studies (P<0.05, all; **Figure 2**)

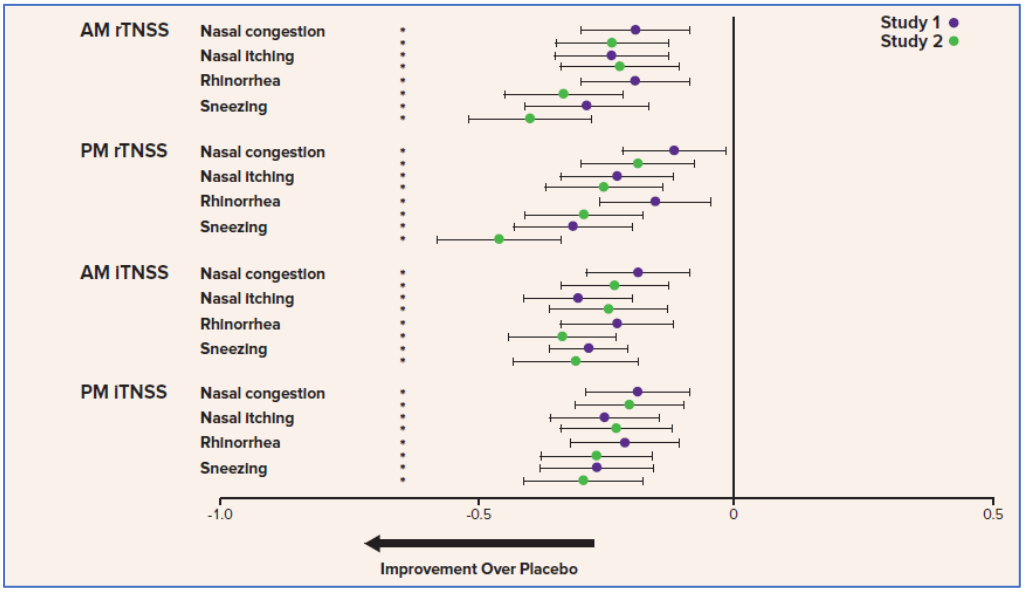
Table 1. Mean Difference in Average AM and Average PM rTNSS and iTNSS With GSP301 Versus Placebo

GSP301 vs Placebo	n1, n2	LSMD	95% CI	*P* value
Average AM rTNSS				
Study 1	299, 283	-0.90	-1.22, -0.59	<0.001*
Study 2	291, 290	-1.19	-1.60, -0.78	<0.001*
Average PM rTNSS				
Study 1	299, 283	-0.75	-1.14, -0.36	<0.001*
Study 2	291, 291	-1.16	-1.56, -0.75	<0.001*
Average AM iTNSS				
Study 1	299, 283	-1.07	-1.19, -0.95	<0.001*
Study 2	291, 290	-1.10	-1.49, -0.71	<0.001*
Average PM iTNSS				
Study 1	299, 283	-0.97	-1.09, -0.84	<0.001*
Study 2	291, 291	-0.95	-1.35, -0.56	<0.001*

GSP301, olopatadine 665 µg/mometasone 25 µg; placebo, GSP301 vehicle.
* Indicates statistical significance (P<0.05) versus placebo.
CI, confidence interval; FAS, full analysis set; LSMD, least squares mean difference; iTNSS, instantaneous Total Nasal Symptom Score; rTNSS, reflective Total Nasal Symptom Score.

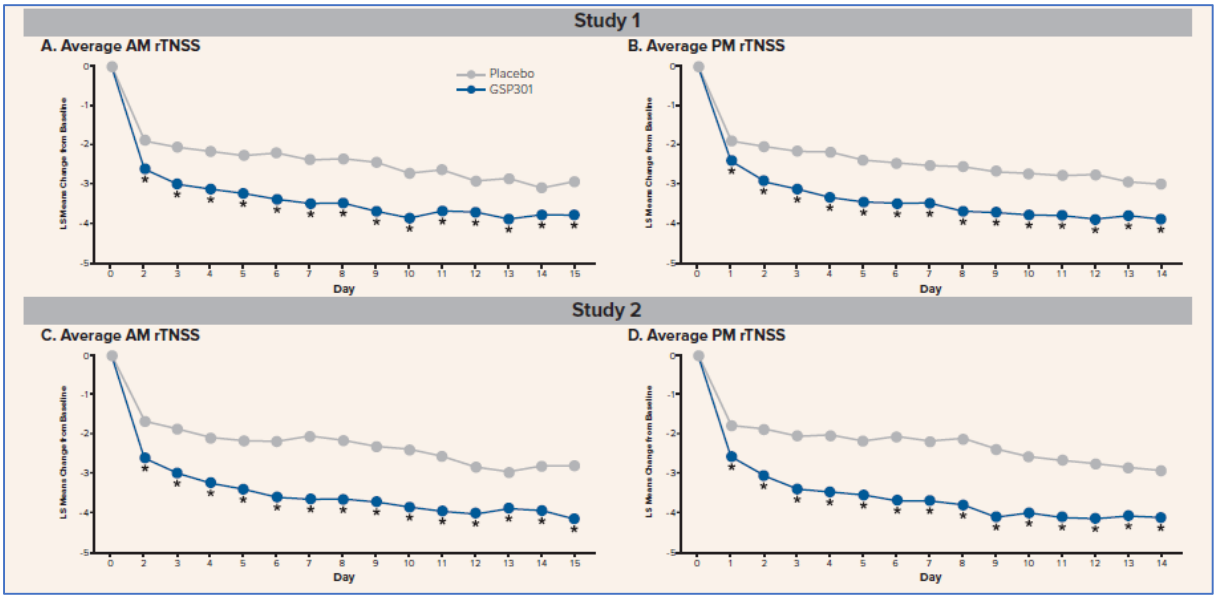
- Further, GSP301 improved average AM and average PM rTNSS (**Figure 3**) and iTNSS (**Figure 4**) on each of the 14 treatment days in both studies versus placebo
- GSP301 provided significant improvements in average AM rTNSS on all treatment days in Study 1 (P<0.01, all; Figure 3A); on the average PM rTNSS, improvements on days 2-14 were also significant (P≤0.001, all), with day 1 approaching statistical significance (P=0.073; **Figure 3B**)
- Improvements on the average AM and average PM rTNSS were significant on all treatment days in Study 2 (P<0.001, all; **Figures 3C and 3D**)
- Similarly, improvements on the average AM and average PM iTNSS were significant on all treatment days in both studies (P≤0.01, all; **Figures 4A, B, C, and D**)

Figure 2. LS Mean Difference (95% CI) in Average AM and Average PM rTNSS and iTNSS Individual Nasal Symptoms With GSP301 Versus Placebo (FAS)



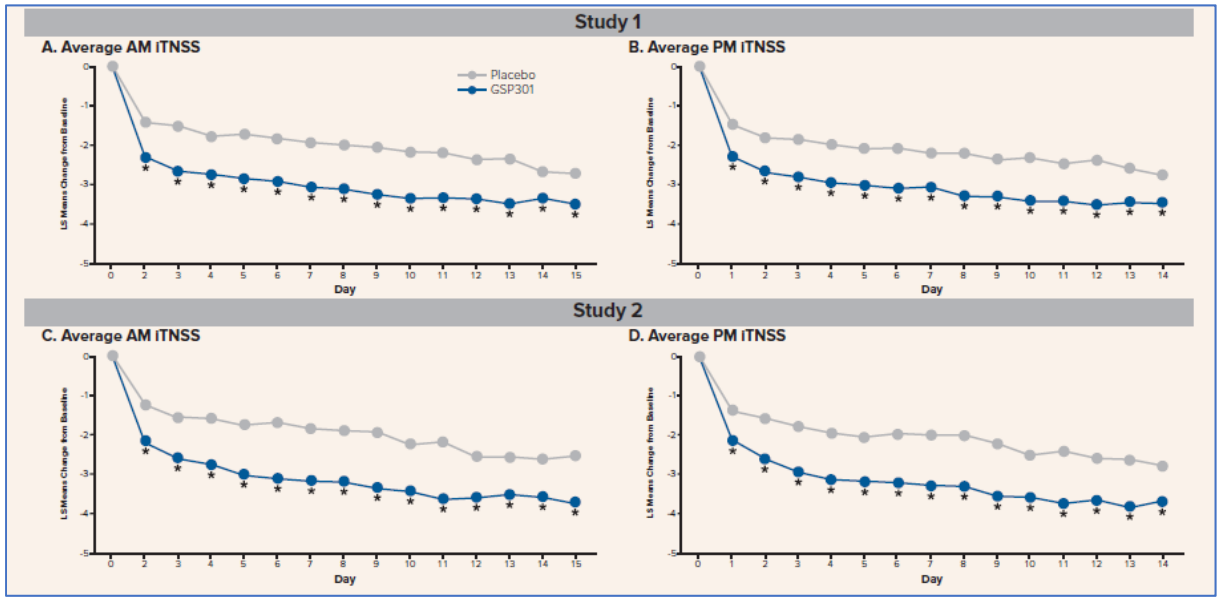
GSP301, olopatadine 665 µg/mometasone 25 µg; placebo, GSP301 vehicle.
* Indicates statistical significance (P<0.05) for GSP301 versus placebo.
Study 1: GSP301 n=299, placebo n=283; Study 2: AM TNSS GSP301 n=291, placebo n=290; PM rTNSS/iTNSS GSP301 n=291, placebo n=291 (except iTNSS sneezing placebo n=290).
CI, confidence interval; FAS, full analysis set; LSMD, least squares mean difference; iTNSS, instantaneous Total Nasal Symptom Score; rTNSS, reflective Total Nasal Symptom Score.

Figure 3. LS Mean Change from Baseline in Average AM and Average PM rTNSS With GSP301 Versus Placebo on Each Day for Study 1 (A and B) and Study 2 (C and D) (FAS)



GSP301, olopatadine 665 µg/mometasone 25 µg; placebo, GSP301 vehicle.
* Indicates statistical significance (P<0.05) for GSP301 versus placebo.
FAS, full analysis set; LS, least squares; rTNSS, reflective Total Nasal Symptom Score.

Figure 4. LS Mean Change from Baseline in Average AM and Average PM iTNSS With GSP301 Versus Placebo on Each Day for Study 1 (A and B) and Study 2 (C and D) (FAS)



GSP301, olopatadine 665 µg/mometasone 25 µg; placebo, GSP301 vehicle.
* Indicates statistical significance (P<0.05) for GSP301 versus placebo.
FAS, full analysis set; LS, least squares; iTNSS, instantaneous Total Nasal Symptom Score.

Safety

- In both studies, a greater percentage of GSP301-treated patients reported a TEAE than placebo-treated patients:
  - Study 1: GSP301 12.9% (n/N: 39/302); placebo 9.4% (27/287)
  - Study 2: GSP301 15.6% (46/294); placebo 9.5% (28/294)
- Most TEAEs were mild or moderate in severity; the most common TEAEs (occurring in ≥2% of patients in any treatment) were dysgeusia and headache
  - One placebo-treated patient in Study 1 discontinued due to a TEAE
- Two patients had serious AEs that were not considered related to treatment: 1 treated with GSP301 in Study 1 (spontaneous abortion) and 1 treated with placebo in Study 2 (osteomyelitis, syncope, and foot fracture)
- No deaths occurred in either study

CONCLUSIONS

- When the average AM and average PM nasal symptoms were analyzed separately in two replicate SAR studies, twice-daily GSP301 resulted in greater improvements versus placebo for both the AM and the PM nasal symptoms
- The significant nasal symptom improvements seen with GSP301 versus placebo in the pre-dose AM and pre-dose PM iTNSS suggest that efficacy was maintained over the entire 12-hour twice-daily dosing interval throughout the 14-day treatment period

REFERENCES

1. Ratner P, et al. 2017. Poster presented at the American College of Allergy, Asthma, and Immunology; October 26-30; Boston, MA.
2. Hampel F, et al. 2018. Poster presented at the American Academy of Allergy, Asthma & Immunology/World Allergy Congress Joint Congress; March 2-5; Orlando, FL.