RAPID NASAL SYMPTOM ONSET OF ACTION AND OCULAR SYMPTOM RELIEF WITH OLOPATADINE/MOMETASONE COMBINATION NASAL SPRAY IN PATIENTS WITH SEASONAL ALLERGIC RHINITIS: A POOLED ANALYSIS

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ABSTRACT

Introduction

GSP301, a fixed-dose combination nasal spray containing olopatadine hydrochloride (antihistamine) and mometasone furoate (corticosteroid), was efficacious for treating seasonal allergic rhinitis (SAR) nasal and ocular symptoms, with a rapid onset of action (OOA), and was well tolerated (previously reported). Pooled analysis of OOA and ocular symptoms from 3 SAR studies are reported here.

Methods

Twice-daily treatment results were pooled from double-blind, randomized, placebo-controlled, 14-day studies (NCT02318303, NCT02631551, NCT02870205; N=2,971). SAR patients (12–65 years) were equally randomized to twice-daily GSP301 (olopatadine 665 µg and mometasone 25 µg), olopatadine (665 µg), mometasone (25 µg), or placebo. Results from once-daily treatments, evaluated only in NCT02318303, are not shown here. OOA (mean change from baseline in instantaneous Total Nasal Symptoms Scores from 15 minutes to 4 hours post-dose vs placebo) was analyzed using mixed-effect model repeated measures (MMRM; $P<0.05$=statistically significant). Average of AM and PM 12-hour reflective Total Ocular Symptom Scores (rTOSS) was also assessed.

Results

GSP301 OOA was observed at 15 minutes post-dose (least squares mean difference [95% CI]: -0.23 [-0.41, -0.05], $P=0.011$); at all 9 subsequent timepoints, OOA was maintained and differences were clinically meaningful and significant ($P<0.001$, all). GSP301 significantly improved rTOSS vs placebo from baseline to day 14 (-0.47 [-0.66, -0.28] $P<0.001$) and on each day (1-14; $P<0.001$, all). Treatment-emergent adverse events were low and comparable across treatments (reported elsewhere).

Conclusion

Twice-daily GSP301 provided rapid OOA of 15 minutes, statistically significant ocular symptom improvements, and was well tolerated in a pooled analysis of SAR studies conducted across different pollen seasons.

PRESENTED AT THE ANNUAL EASTERN ALLERGY CONFERENCE
MAY 30-JUNE 2, 2019 I PALM BEACH, FL

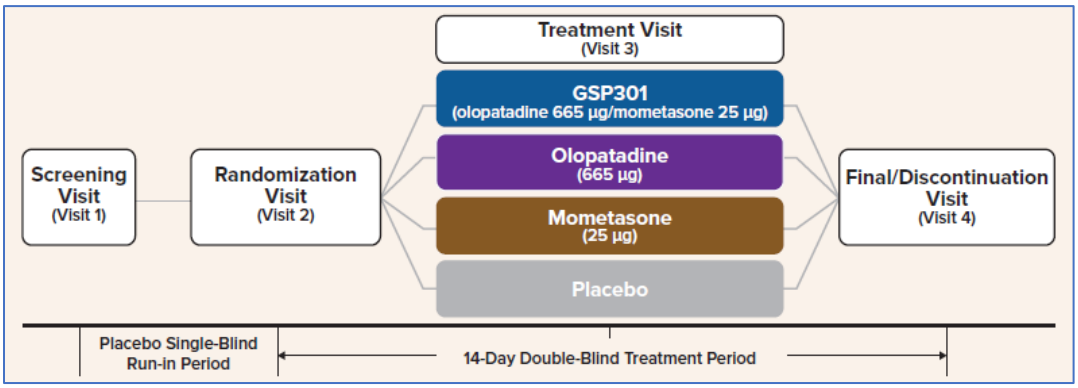
PREVIOUSLY PRESENTED AT:
THE AMERICAN ACADEMY OF ALLERGY, ASTHMA, AND IMMUNOLOGY
FEBRUARY 22-25, 2019 I SAN FRANCISCO, CA

KEY FINDINGS

STUDY DESIGN

- Efficacy results were pooled from 3 randomized, double-blind, placebo-controlled (RDBPC), 14-day SAR studies: Study 1 (NCT02318303; phase 2) and Studies 2 and 3 (NCT02631551 and NCT02870205; phase 3 replicate studies) conducted with different seasonal allergens (**Figure 1**)
- Safety results were pooled from the three RDBPC studies (as above) plus a 14-day double blind, randomized, double-dummy proof-of-concept study (Study 4; NCT03444506) conducted in an environmental exposure chamber (EEC)
- In all four studies, patients self-administered study medication and, twice daily, self assessed reflective and instantaneous nasal symptoms (nasal congestion, itchy nose, rhinorrhea, and sneezing) and ocular symptoms (itching/burning, tearing/watering, and redness of eyes) in a symptom diary
- Efficacy procedures in Study 4 differed from the RDBPC studies (EEC vs natural allergen exposure design) but treatment exposure time was the same (14 days), thus only the safety data from Study 4 were included in the pooled analysis presented here (efficacy data previously published[1])

Figure 1. Study Design: Pooled Efficacy Data (Studies 1, 2, and 3)



All treatments were self-administered as two sprays per nostril twice daily; additional treatments dosed once daily (Study 1) were not included in the pooled analysis and are not shown here (see Methods for details).
See Methods for Study 4 design (not shown here); only safety data were included in the pooled analysis.

Endpoints

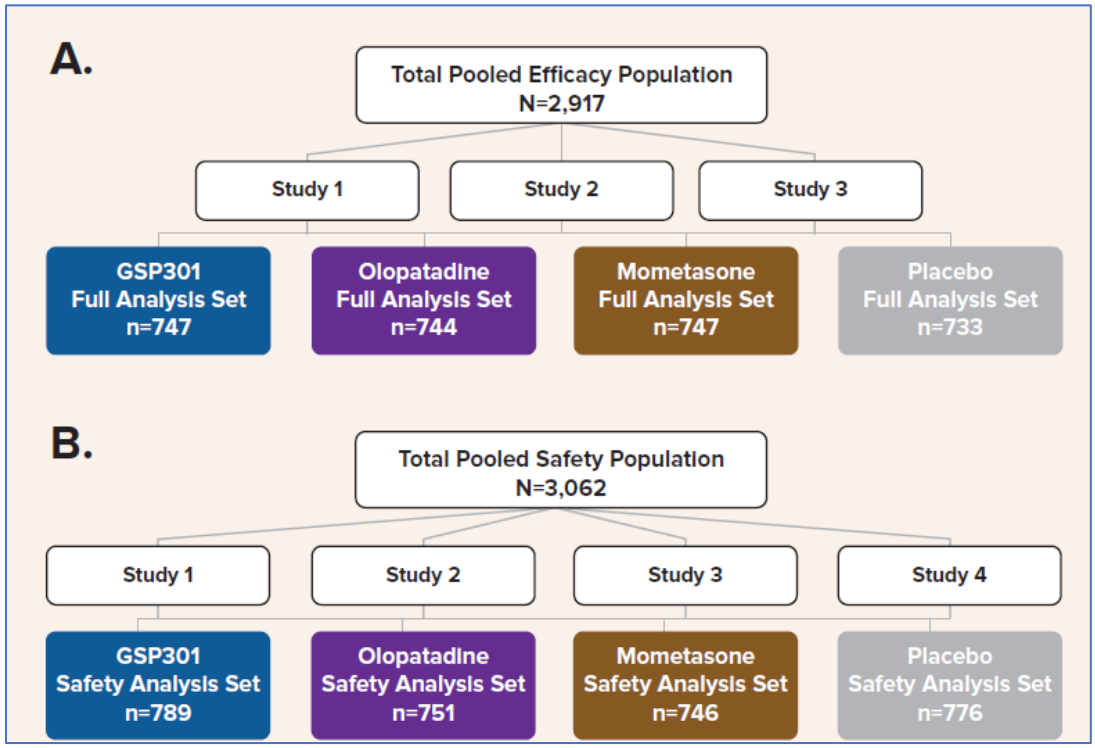
- Pooled efficacy analysis (Studies 1, 2 and 3):
  - Onset of action was assessed based on mean change from baseline in instantaneous Total Nasal Symptom Score (iTNSS) from 15 minutes to 4 hours after the first dose administered (11 timepoints total)
  - Ocular symptoms were evaluated through mean change from baseline to end of 14-day treatment in average of AM and PM 12-hour reflective Total Ocular Symptom Score (rTOSS)
- Pooled safety analysis (Studies 1, 2, 3 and 4):
  - Safety was monitored via adverse events (AEs), laboratory assessments, vital signs, physical examinations, ear, nose and throat examinations, and electrocardiograms
- The pooled analysis of the primary and secondary endpoints—mean change from baseline to the end of treatment in patient-reported AM and PM 12-hour rTNSS and iTNSS, respectively—and detailed safety outcomes have been reported in the TNSS poster
- Only data pertaining to twice-daily GSP301 and placebo treatments are reported here

RESULTS

Patients

- A total of 2,971 patients were included in the pooled efficacy analysis (FAS; **Figure 2A**)
- Most patients were female with a mean age ranging from 40.2 to 40.5 years and had moderate to severe symptoms (**Table 1**)
- Demographic characteristics and baseline nasal and ocular symptom scores (FAS) were similar across the treatment groups (**Table 1**)

Figure 2. Pooled Efficacy (A) and Safety (B) Populations



GSP301, olopatadine 665 µg and mometasone 25 µg; olopatadine, 665 µg; mometasone, 25 µg; placebo, GSP301 vehicle.

Efficacy

- In the pooled analysis, onset of action for GSP301 was observed at 15 minutes post-dose (first post-dose timepoint; least squares mean difference [95% CI]: -0.23 [-0.41, -0.05], *P*=0.011; **Figure 3**)
  - At all 9 subsequent timepoints, the significant differences between GSP301 and placebo were maintained (*P*<0.001, all) and were clinically meaningful[2]; these results are similar to those seen in two of the individual studies[3,4]
- GSP301 significantly improved average AM and PM rTOSS compared with placebo from baseline to end of treatment (-0.47 [-0.66, -0.28], *P*<0.001) in the pooled analysis (**Figure 4**)
- In the pooled analysis, GSP301 showed significant improvements in average AM and PM rTOSS vs placebo on day 1 and each subsequent day (days 1-14; *P*<0.001, all) suggesting sustained ocular symptom improvement (**Figure 5**)
- Treatment comparisons of the average AM and PM 12-hour rTOSS over 14 days for the individual studies, as well as the pooled analysis, are shown in **Figure 4** (results for the individual studies have been published elsewhere[3,4])

KEY FINDINGS

Table 1. Demographics and Baseline Symptom Scores (FAS) – Pooled Analysis

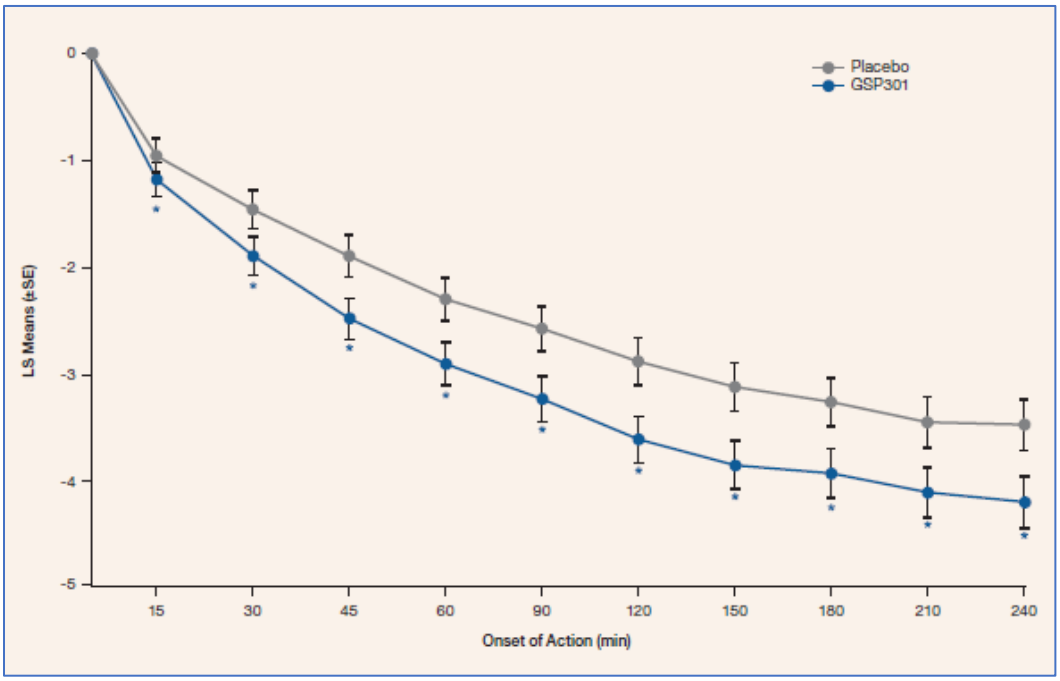
Demographics	GSP301 (n=747)	Placebo (n=733)
Age, mean ± SD, y	40.2 ± 15.0	40.5 ± 15.1
Sex, n (%)		
Female	512 (68.5)	466 (63.6)
Male	235 (31.5)	267 (36.4)
Race, n (%)		
White	617 (82.6)	590 (80.5)
Black	108 (14.5)	129 (17.6)
Other[a]	22 (2.9)	14 (1.9)
Ethnicity, n (%)		
Non-Hispanic or Latino	529 (70.8)	531 (72.4)
Hispanic or Latino	218 (29.2)	202 (27.6)
BMI, mean ± SD, kg/m^2	30.1 ± 8.7	30.0 ± 9.2
Baseline symptom scores, mean ± SD		
Average AM and PM 12-hour iTNSS	9.3 ± 1.8	9.5 ± 1.7
Average AM and PM 12-hour rTOSS	7.1 ± 1.4	7.2 ± 1.4

GSP301, olopatadine 665 µg and mometasone 25 µg; placebo, GSP301 vehicle. Pooled efficacy data from Studies 1, 2, and 3. Demographics for the SAS population are shown in the TNSS poster.

[a] Includes Asian, American Indian or Alaska native, and native Hawaiian or other Pacific Islander.

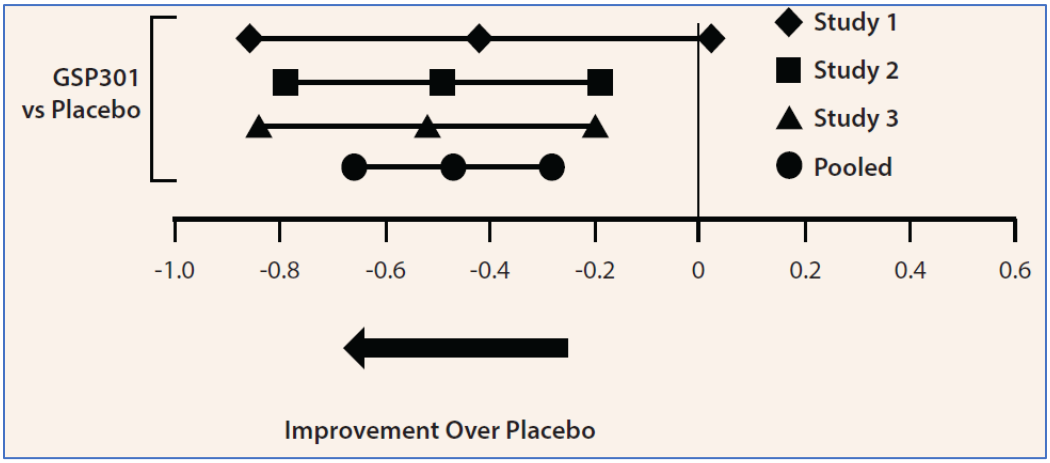
BMI, body mass index; FAS, full analysis set; iTNSS, instantaneous Total Nasal Symptom Score; rTOSS, reflective Total Ocular Symptom Score; SD, standard deviation.

Figure 3. Average iTNSS Onset of Action by Timepoint (FAS) – Pooled Analysis



GSP301, olopatadine 665 µg and mometasone 25 µg; placebo, GSP301 vehicle. Pooled efficacy data from Studies 1, 2, and 3.
* Indicates statistical significance ($P<0.05$) vs placebo.
FAS, full analysis set; iTNSS, instantaneous Total Nasal Symptom Score; LS, least squares; SE, standard error.

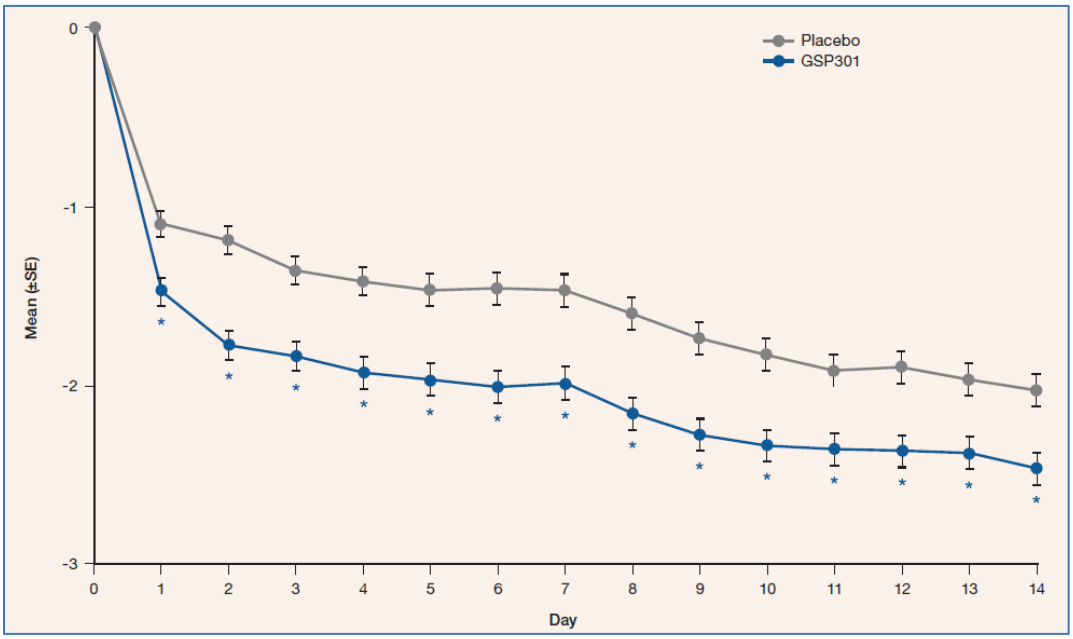
Figure 4. Treatment Comparisons of Average AM and PM 12-hour rTOSS Over 14 Days for the Pooled Analysis and Individual Studies (FAS)



GSP301, olopatadine 665 µg and mometasone 25 µg; placebo, GSP301 vehicle.
Efficacy data are presented from each individual study and the pooled studies (Studies 1, 2, and 3).
Data are presented as least squares mean difference with 95% CIs.
CI, confidence interval; FAS, full analysis set; rTOSS, reflective Total Ocular Symptom Score.

KEY FINDINGS

Figure 5. Mean Change from Baseline in Average AM and PM 12-hour rTOSS by Day (FAS) – Pooled Analysis



GSP301, olopatadine 665 µg and mometasone 25 µg; placebo, GSP301 vehicle. Pooled efficacy data from Studies 1, 2, and 3.
* Indicates statistical significance (P<0.05) vs placebo.
FAS, full analysis set; rTOSS, reflective Total Ocular Symptom Score; SE, standard error.

Safety

- Detailed safety data for the four pooled studies have been reported in the TNSS poster
  - Treatment-emergent AE (TEAE) rates were 13.9% (n/N: 110/798) for GSP301 and 9.5% (74/776) for placebo; most were mild-moderate in severity
  - Only one serious AE (SAE) led to study discontinuation (foot fracture in the placebo group) and no SAEs were considered related to treatment; no deaths occurred

CONCLUSIONS

- In a pooled efficacy analysis of 3 SAR studies conducted with different seasonal allergens, twice-daily GSP301 treatment:
  - Provided a rapid onset of action of 15 minutes vs placebo that was maintained across all subsequent timepoints
  - Significantly improved reflective ocular symptoms compared with placebo
- In a pooled safety analysis of 4 SAR studies, GSP301 was well tolerated, with TEAE rates that were generally low and similar across treatments

REFERENCES

1. Patel P, et al. *Ann Allergy Asthma Immunol.* 2018;122(2):160-166.
2. Barnes ML, et al. *Clin Exp Allergy.* 2010;40(2):242-250.
3. Gross G, et al. *Ann Allergy Asthma Immunol.* 2019;S1081-1206(19):30196-6.
4. Hampel F, et al. *Allergy Asthma Proc.* 2019; https://www.ncbi.nlm.nih.gov/pubmed/31053180. Accessed May 15, 2019