RAPID ONSET OF ACTION AND IMPROVEMENT OF NASAL AND OCULAR SYMPTOMS WITH OLOPATADINE/MOMETASONE COMBINATION NASAL SPRAY IN PATIENTS WITH SEASONAL ALLERGIC RHINITIS

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ABSTRACT

Objective

In two randomized double-blind studies, twice-daily GSP301 nasal spray—a fixed-dose combination of olopatadine hydrochloride and mometasone furoate—significantly improved reflective total nasal symptom scores (rTNSS) vs placebo (primary endpoint; presented elsewhere). GSP301 onset of action and reflective total ocular symptom scores (rTOSS) are presented here.

Methods

In each study (study 1 [NCT02631551]; study 2 [NCT02870205]), patients ≥12 years with Seasonal Allergic Rhinitis (SAR) were equally randomized to GSP301 (olopatadine 665µg/mometasone 25µg BID), olopatadine (665µg BID), mometasone (25µg BID), or placebo for 14 days. GSP301 onset of action was assessed by mean change from baseline in average instantaneous TNSS (iTNSS) at various timepoints (from 15 minutes to 4 hours post-dose) vs placebo and analyzed via mixed-effect model repeated measures, adjusting for covariates.

Results

A total of 1,180 and 1,176 patients were randomized in studies 1 and 2, respectively. A rapid onset of action for GSP301 was observed at 15 minutes post-dose vs placebo in study 1 (least squares mean difference [95% CI]: -0.35 [-0.63, -0.07]; *P*=0.014) and study 2 (-0.34 [-0.65, -0.04]; *P*=0.028), an effect that was maintained at each subsequent timepoint assessed. Additionally, GSP301 statistically significantly improved rTOSS vs placebo in both studies (study 1: *P*=0.0014; study 2: *P*=0.001). Treatment-emergent adverse events were low and comparable across treatments.

Conclusions

In two SAR studies, GSP301 BID treatment had a rapid onset of action of 15 minutes, provided significant improvements in ocular symptoms versus placebo, and was well tolerated.

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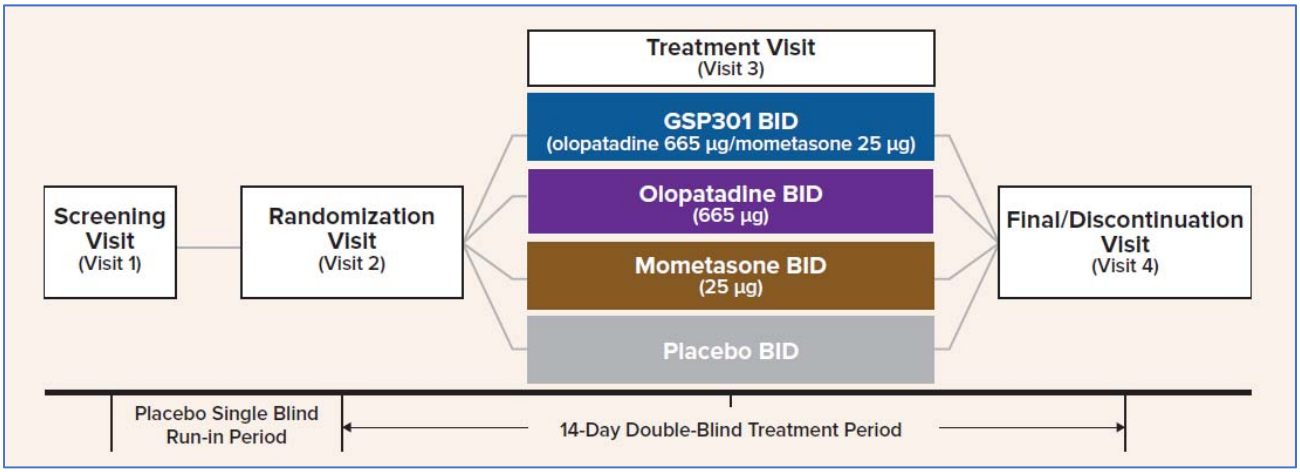
KEY FINDINGS

STUDY DESIGN

- Two similarly designed double-blind, randomized, parallel-group studies (Study 1 [NCT02631551]; Study 2 [NCT02870205]) were conducted in patients with SAR during the Spring (Study 1) and Fall/mountain cedar (Study 2) pollen seasons
- 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
- Onset of action was evaluated based on changes in self-assessed nasal symptoms at 11 timepoints after the first dose administered (visit 2)

Figure 1. Study Design



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.
BID, twice-daily dosing.

Endpoints

- Onset of action was evaluated based on mean change from baseline in iTNSS from 15 minutes to 4 hours (11 timepoints) after the first dose administered at the study site (visit 2) compared with placebo (**Figure 2**)
- Ocular symptoms were assessed through mean change from baseline to end of treatment (visit 4) in post-dose rTOSS vs placebo
- AEs were also evaluated
- 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—for both trials has been reported elsewhere[1,2]
- Only data pertaining to GSP301 and placebo are reported here

RESULTS

Patients

- A total of 1,180 and 1,176 patients were randomized in Studies 1 and 2, respectively
- At baseline, patients had moderate to severe symptoms, with mean rTNSS ranging from 10.1 to 10.3 and mean iTNSS ranging from 9.2 to 9.4 (**Table 1**)

Table 1. Baseline Characteristics

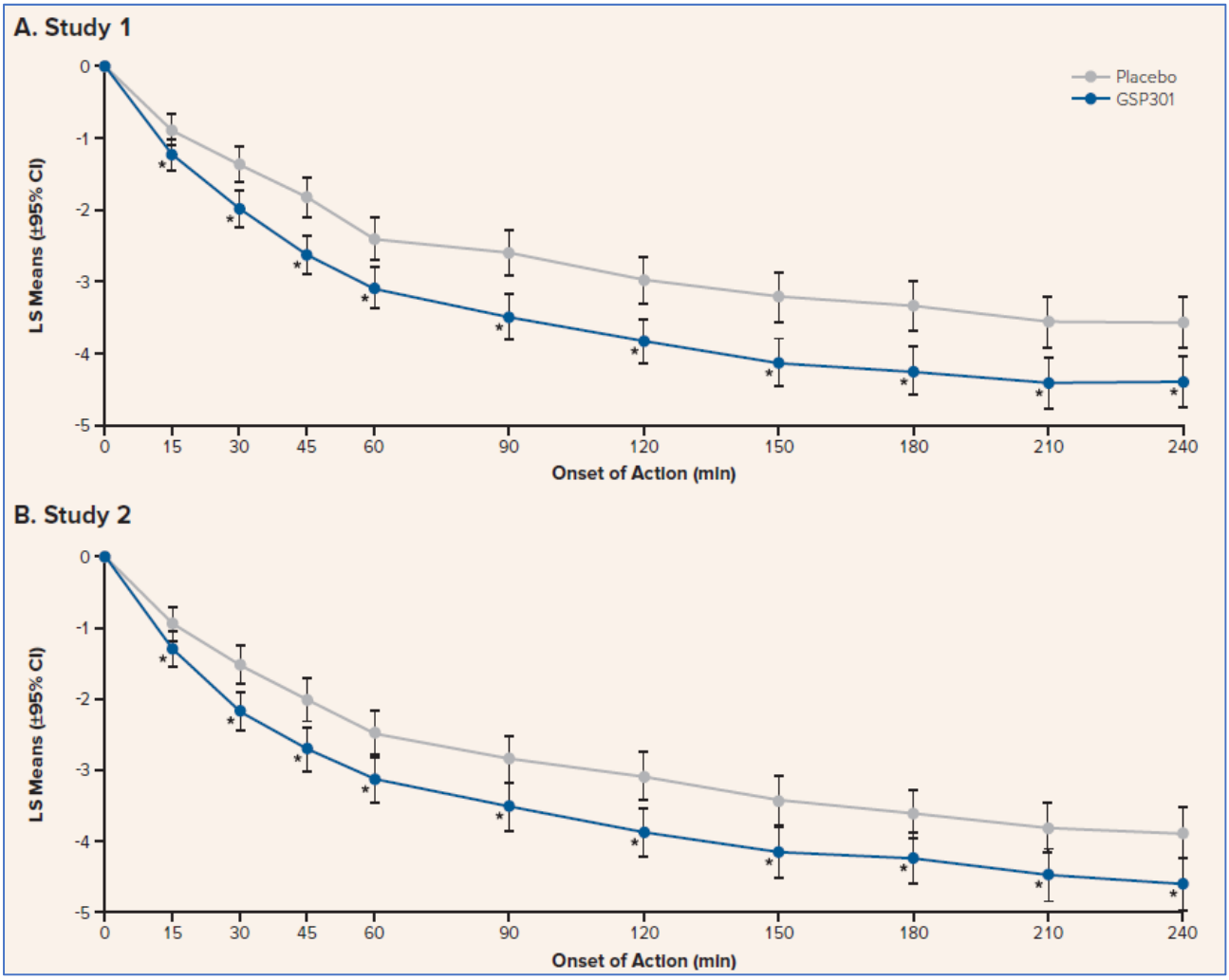
	Study 1		Study 2	
	GSP301 (n=302)	Placebo (n=287)	GSP301 (n=294)	Placebo (n=294)
Demographics				
Age, mean ± SD, y	39.5 ± 15.4	39.4 ± 14.8	39.9 ± 14.9	39.6 ± 14.9
Sex, n (%)				
Male	101 (33.4)	105 (36.6)	91 (31.1)	117 (39.9)
Female	201 (66.6)	182 (63.4)	202 (68.9)	176 (60.1)
Race, n (%)				
White	241 (79.8)	231 (80.5)	251 (85.7)	229 (78.2)
Black	56 (18.5)	48 (16.7)	30 (10.2)	60 (20.5)
Asian	2 (0.7)	7 (2.4)	7 (2.4)	3 (1.0)
Other[a]	3 (1.0)	1 (0.3)	5 (1.7)	1 (0.3)
Ethnicity, n (%)				
Non-Hispanic or Latino	230 (76.2)	221 (77.0)	224 (76.5)	214 (73.0)
Hispanic or Latino	72 (23.8)	66 (23.0)	69 (23.5)	79 (27.0)
Baseline Clinical Characteristics				
rTNSS, mean ± SD[b]	10.1 ± 1.2	10.2 ± 1.2	10.1 ± 1.2	10.3 ± 1.2
iTNSS, mean ± SD[b]	9.2 ± 1.7	9.3 ± 1.7	9.2 ± 1.8	9.6 ± 1.8
rTOSS, mean ± SD[b]	7.1 ± 1.4	7.2 ± 1.3	7.0 ± 1.5	7.2 ± 1.4

GSP301, olopatadine 665 µg/mometasone 25 µg BID.
[a]Includes American Indian or Alaska native, native Hawaiian or other Pacific Islander.
[b]Full analysis set; Study 1: GSP301 n=299; placebo n=283; Study 2: GSP301 n=292; placebo n=291.
BID, twice-daily dosing; iTNSS, instantaneous Total Nasal Symptom Score; rTNSS, reflective Total Nasal Symptom Score; rTOSS, reflective Total Ocular Symptom Score; SD, standard deviation.

Efficacy

- In both studies, a rapid onset of action with GSP301 treatment was demonstrated at 15 minutes after the first dose versus placebo
  - Study 1 LSMD [95% CI]: -0.35 [-0.63, -0.07]; *P*=0.014
  - Study 2 LSMD [95% CI]: -0.34 [-0.65, -0.04]; *P*=0.028
- The significant improvement (statistically significant, *P*<0.05) in iTNSS observed at 15 minutes after first dose was maintained at each subsequent timepoint assessed (**Figure 2**)

Figure 2. LS Means (95% CI) of Change from Baseline in Average iTNSS Onset of Action for Studies 1 (A) and 2 (B)



GSP301, olopatadine 665 µg/mometasone 25 µg BID.
*P<0.05 vs placebo.
BID, twice-daily dosing; CI, confidence interval; iTNSS, instantaneous Total Nasal Symptom Score; LS, least squares; min, minutes.

- In both studies, GSP301 significantly improved ocular symptoms (rTOSS) versus placebo (*P*=0.001 for both studies; **Table 2**)

Table 2. LS Mean Difference in Average AM and PM rTOSS with GSP301 vs Placebo Over the 14-day Treatment Period

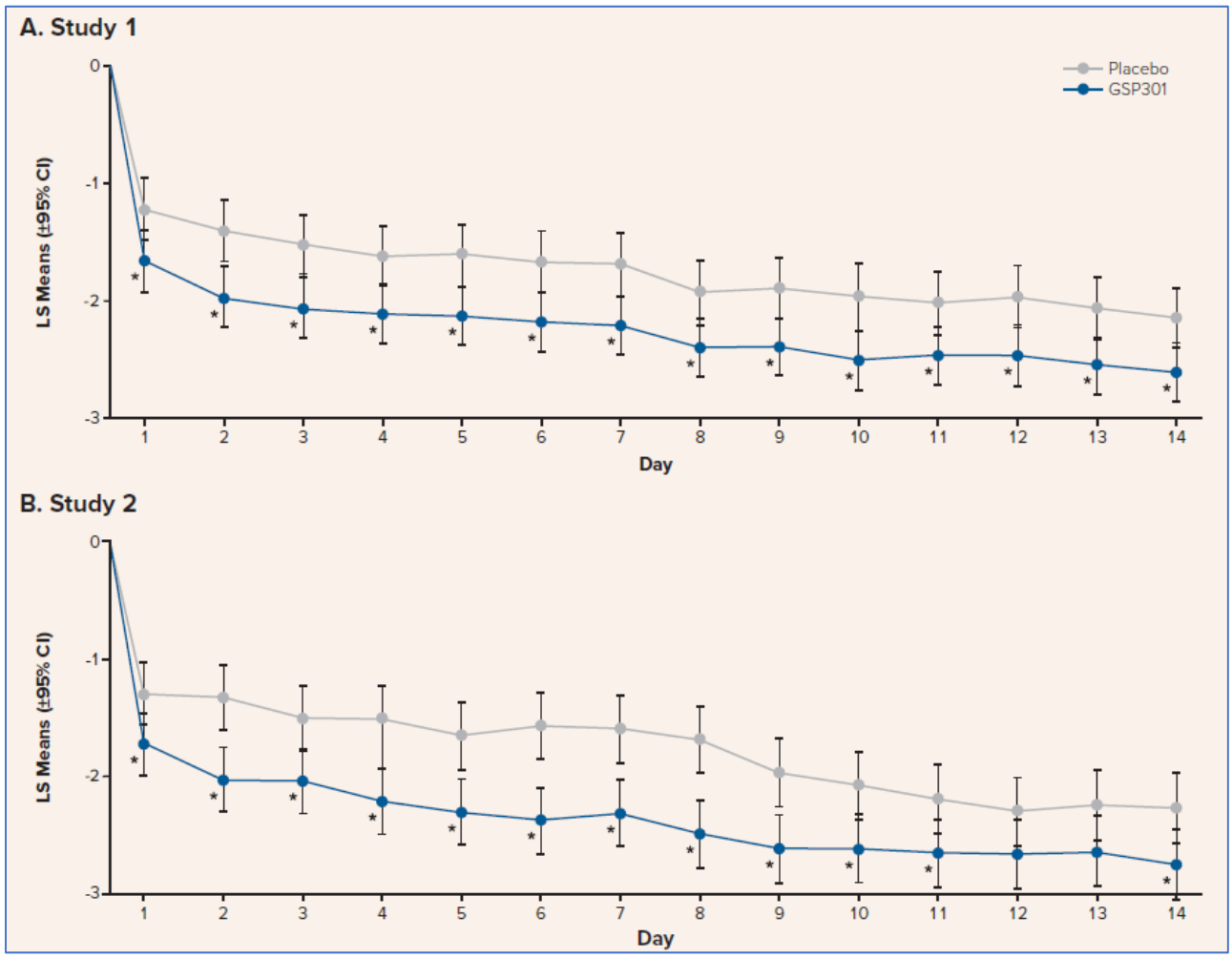
GSP301 vs Placebo	n1, n2	LSMD	95% CI	*P* value
Study 1	299, 283	-0.49	-0.79, -0.19	0.001*
Study 2	291, 290	-0.52	-0.84, -0.20	0.001*

GSP301, olopatadine 665 µg/mometasone 25 µg BID.
*Indicates significant P values vs placebo.
BID, twice-daily dosing; CI, confidence interval; LS, least squares; LSMD, least squares mean difference; rTOSS, reflective Total Ocular Symptom Score.

KEY FINDINGS

- GSP301 significantly improved rTOSS versus placebo on each day in both studies, except on days 12 (*P*=0.085) and 13 (*P*=0.055) in Study 2 (*P*<0.05, all; **Figure 3**), suggesting sustained symptom improvement

Figure 3. LS Means (95% CI) of Change from Baseline in Average AM and PM rTOSS with GSP301 vs Placebo for Each Day for Studies 1 (A) and 2 (B)



GSP301, olopatadine 665 µg/mometasone 25 µg BID.
*P<0.05 vs placebo.
BID, twice-daily dosing; CI, confidence interval; LS, least squares; rTOSS, reflective Total Ocular Symptoms Score.

KEY FINDINGS

Safety

- The majority of TEAEs were mild or moderate in severity and were not considered related to treatment (**Table 3**)

Table 3. Adverse Events

n, (%)	Study 1		Study 2	
	GSP301 (n=302)	Placebo (n=287)	GSP301 (n=294)	Placebo (n=294)
Patients reporting ≥1 TEAE	39 (12.9)	27 (9.4)	46 (15.6)	28 (9.5)
TEAEs[a]				
Dysgeusia	10 (3.3)	2 (0.7)	11 (3.7)	0 (0)
Headache	2 (0.7)	8 (2.8)	0 (0)	2 (0.7)
Patients with a TEAE leading to withdrawal	0 (0)	1 (0.3)	0 (0)	0 (0)
Patients with an SAE	1 (0.3)	0 (0)	0 (0)	1 (0.3)
Deaths	0 (0)	0 (0)	0 (0)	0 (0)

GSP301, olopatadine 665 µg/mometasone 25 µg BID.
[a]Occurring in ≥2% of patients in any treatment group.
BID, twice-daily dosing; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- In two replicate SAR studies, twice-daily (BID) GSP301 treatment demonstrated a rapid onset of action of 15 minutes, which was maintained at subsequent timepoints
- GSP301 also provided significant, sustained improvements in SAR ocular symptoms versus placebo
- Only mild to moderate AEs were reported with GSP301 treatment
- These results demonstrate that GSP301 BID is well tolerated and provides rapid and sustained relief of SAR symptoms in adolescent and adult patients 12 years of age and older

REFERENCES

1. Hampel F, et al. 2018. Poster presented at the American Academy of Allergy, Asthma & Immunology (AAAAI) & World Allergy Congress (WAO) Joint Congress; Orlando, FL.
2. Ratner P, et al. 2017. Poster presented at: 75th annual meeting of the American College of Allergy, Asthma, & Immunology; Boston, MA.