

# 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 Score (rTNSS) versus 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  $\geq 12$  years with Seasonal Allergic Rhinitis (SAR) were equally randomized to GSP301 (olopatadine 665  $\mu\text{g}$ /mometasone 25  $\mu\text{g}$  BID), olopatadine (665  $\mu\text{g}$  BID), mometasone (25  $\mu\text{g}$  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) versus 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 versus 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. Additionally, GSP301 statistically significantly improved rTOSS versus placebo (study 1: -0.49 [-0.79, -0.19],  $P=0.0014$ ; study 2: -0.52 [-0.84, -0.20],  $P=0.001$ ). 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.

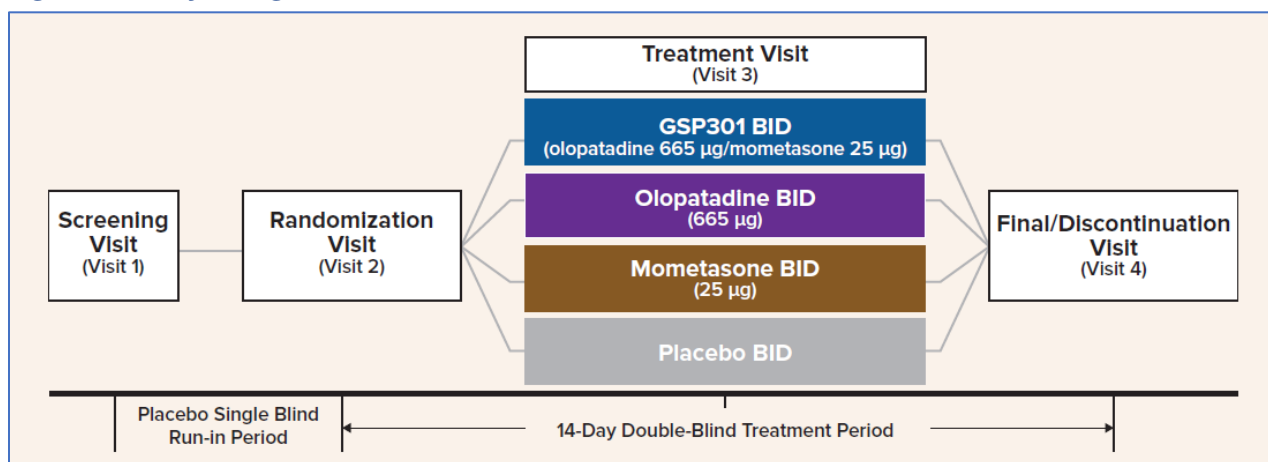
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## STUDY DESIGN

- Two similarly designed double-blind, randomized, parallel-group studies (Study 1 [NCT02631551]; Study 2 [NCT02870205]) were conducted in patients  $\geq 12$  years of age 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<sup>1,2</sup>
- 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, mean iTNSS ranging from 9.2 to 9.4, and mean rTOSS ranging from 7.0 to 7.2 (**Table 1**)

Table 1. Baseline Characteristics

	Study 1		Study 2	
	GSP301 (n=302)	Placebo (n=287)	GSP301 (n=294)	Placebo (n=294)
<b>Demographics</b>				
Age, mean $\pm$ SD, y	39.5 $\pm$ 15.4	39.4 $\pm$ 14.8	39.9 $\pm$ 14.9	39.6 $\pm$ 14.9
<b>Sex, n (%)</b>				
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)
<b>Race, n (%)</b>				
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 <sup>a</sup>	3 (1.0)	1 (0.3)	5 (1.7)	1 (0.3)
<b>Ethnicity, n (%)</b>				
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)
<b>Baseline Clinical Characteristics</b>				
rTNSS, mean $\pm$ SD <sup>b</sup>	10.1 $\pm$ 1.2	10.2 $\pm$ 1.2	10.1 $\pm$ 1.2	10.3 $\pm$ 1.2
iTNSS, mean $\pm$ SD <sup>b</sup>	9.2 $\pm$ 1.7	9.3 $\pm$ 1.7	9.2 $\pm$ 1.8	9.6 $\pm$ 1.8
rTOSS, mean $\pm$ SD <sup>b</sup>	7.1 $\pm$ 1.4	7.2 $\pm$ 1.3	7.0 $\pm$ 1.5	7.2 $\pm$ 1.4

GSP301, olopatadine 665  $\mu$ g/mometasone 25  $\mu$ g BID.

<sup>a</sup>Includes American Indian or Alaska native, native Hawaiian or other Pacific Islander.

<sup>b</sup>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;

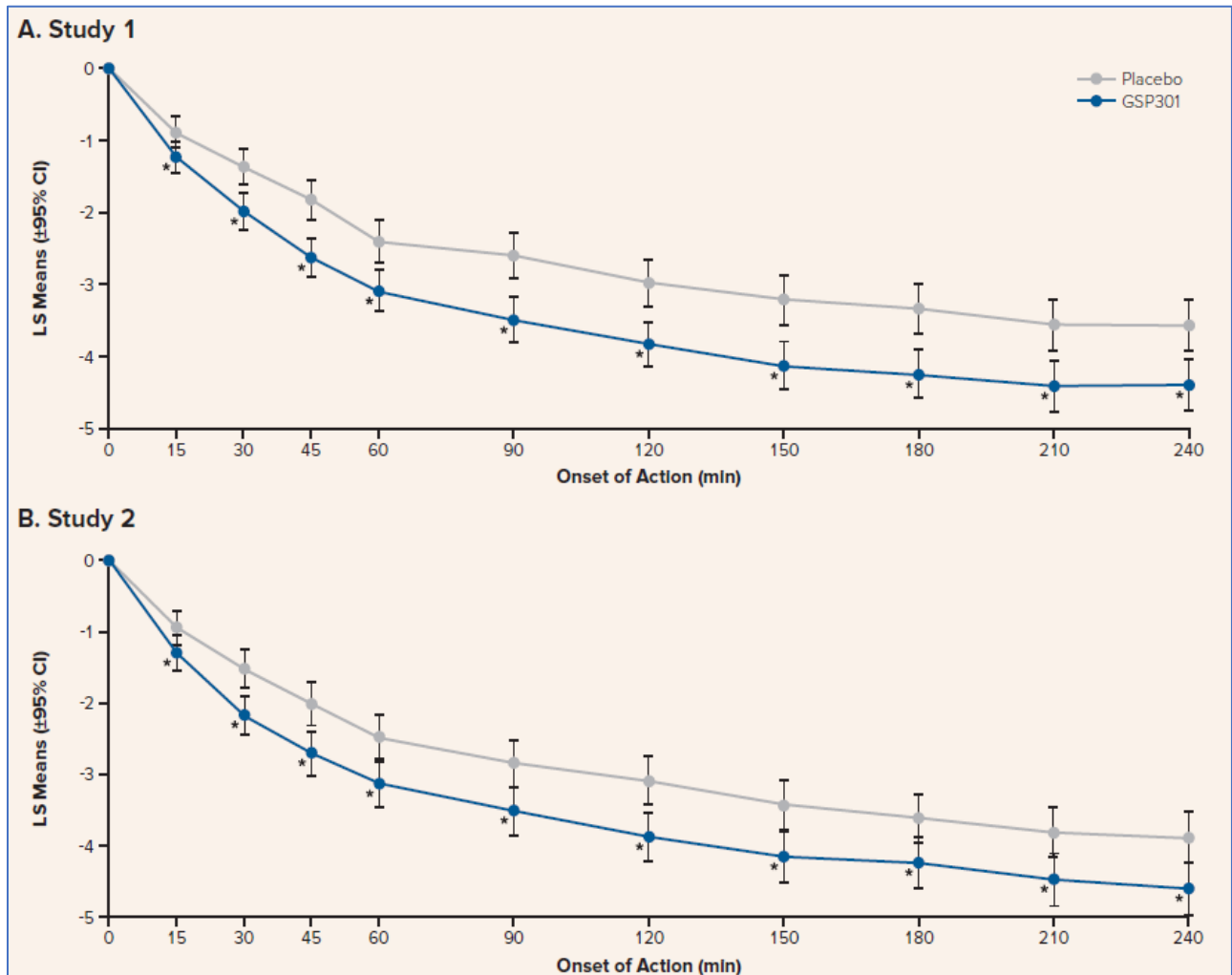
rTOSS, reflective Total Ocular Symptom Score; SD, standard deviation.

## 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**)

# KEY FINDINGS

**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.

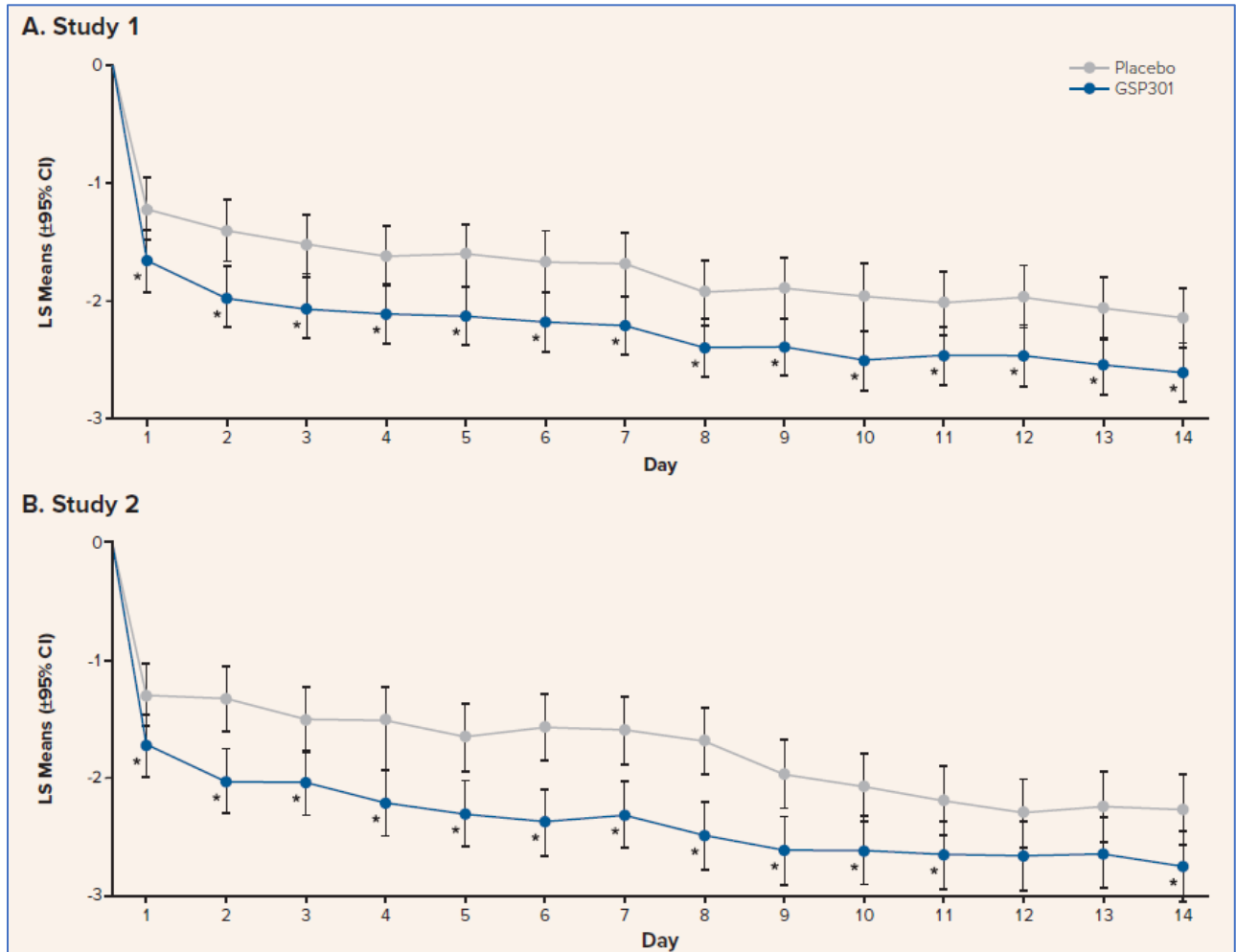
\*Indicates significant P values vs placebo.

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; no deaths occurred (**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)
<b>TEAEs<sup>a</sup></b>				
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.

<sup>a</sup>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.