

EFFICACY AND SAFETY OF OLOPATADINE/MOMETASONE COMBINATION NASAL SPRAY FOR THE TREATMENT OF SEASONAL ALLERGIC RHINITIS

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ABSTRACT

Objective

Combining an intranasal antihistamine with an intranasal corticosteroid for the treatment of allergic rhinitis (AR) may provide improved symptom relief over treatment with either drug alone. GSP301 nasal spray (NS) is a fixed-dose combination of the antihistamine olopatadine hydrochloride and the corticosteroid mometasone furoate. Efficacy and safety of GSP301 were evaluated in this Seasonal AR (SAR) study.

Methods

In this randomized, double-blind, parallel-group study, eligible patients (≥ 12 years) with SAR were randomized 1:1:1:1 to GSP301 (olopatadine 665 μg /mometasone 25 μg BID), olopatadine (665 μg BID), mometasone (25 μg BID), or placebo for 14 days of treatment. The primary endpoint—mean change from baseline in AM and PM reflective Total Nasal Symptom Score (rTNSS)—was analyzed via mixed-effect model repeated measures (MMRM). Adverse events (AEs) were also assessed.

Results

A total of 1,176 patients were randomized. GSP301 BID treatment statistically significantly improved rTNSS scores versus placebo (least square means difference [95% CI]: -1.09 [-1.49, -0.69]; $P < 0.001$). GSP301 BID treatment also showed significant improvement versus olopatadine (-0.44 [-0.84, -0.05]; $P = 0.028$) and mometasone (-0.47 [-0.86, -0.08]; $P = 0.019$). Olopatadine and mometasone monotherapies significantly improved rTNSS scores versus placebo (olopatadine: -0.64 [-1.04, -0.25]; $P = 0.001$; mometasone: -0.62 [-1.01, -0.22]; $P = 0.002$). Treatment-emergent AEs were reported by 15.6%, 12.6%, 9.6% and 9.5% of patients in the GSP301, olopatadine, mometasone, and placebo groups, respectively.

Conclusions

In this study, GSP301 BID treatment provided statistically significant and clinically meaningful improvements in SAR symptoms versus placebo and versus individual monotherapies. GSP301 BID treatment was well tolerated.

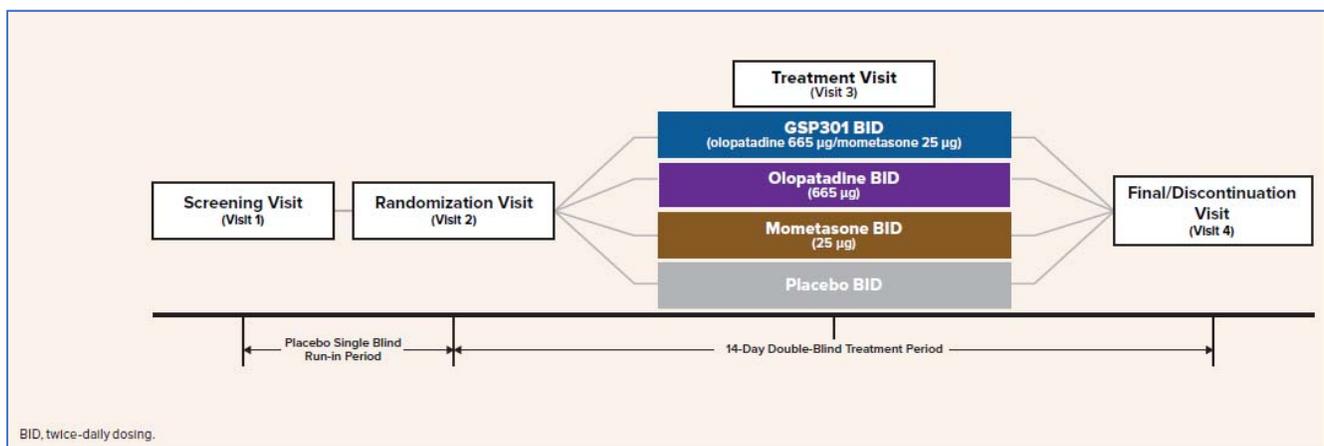
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STUDY DESIGN

- Phase 3, randomized, double-blind, parallel-group study (NCT02631551) in patients with SAR during the Fall and mountain cedar pollen seasons (**Figure 1**)
- Patients ≥ 12 years with a clinical history of SAR for ≥ 2 years self-administered study medication twice-daily and self-assessed AM and PM reflective and instantaneous nasal symptoms (sneezing, runny nose, itchy nose, and nasal congestion) and non-nasal symptoms (itching/burning, tearing/watering, and redness of eyes, and itching of ears or palate) in a symptom diary
- A difference of 0.23 units in TNSS was considered clinically meaningful (defined as the minimal clinically important difference)¹
- Safety was monitored via laboratory and physical examinations, ear, nose and throat examinations, vital signs, ECG, and adverse events (AEs)

Figure 1. Study Design



Endpoints

- Primary: mean change from baseline to end of treatment in patient-reported AM and PM 12-hour rTNSS over the 14-day treatment period for:
 - GSP301 vs placebo
 - GSP301 vs olopatadine and mometasone monotherapies
 - Olopatadine and mometasone monotherapies vs placebo
- Additional: mean change from baseline to end of 14-day treatment in patient-reported AM and PM 12-hour iTNSS; mean AM and PM reflective individual nasal symptoms over the 14-day treatment period; and safety assessments and AEs

RESULTS

Patients

- Efficacy analyses based on the full analysis set (FAS) population, all randomized patients who received ≥ 1 dose of study drug, and completed ≥ 1 post-baseline primary efficacy assessment (n=1,172)
- Safety assessments based on the safety analysis set (SAS), consisting of all patients who received ≥ 1 dose of study drug (n=1,175)
- Demographic and baseline characteristics were comparable among treatment groups (**Table 1**)

KEY FINDINGS

Table 1. Baseline Characteristics

	GSP301 (n=293)	Olopatadine (n=293)	Mometasone (n=293)	Placebo (n=293)
Age, mean ± SD, y	39.9 ± 14.9	39.9 ± 14.6	39.2 ± 14.9	39.6 ± 14.9
Sex, n (%)				
Male	91 (31.1)	104 (35.5)	123 (42.0)	117 (39.9)
Female	202 (68.9)	189 (64.5)	170 (58.0)	176 (60.1)
Race, n (%)				
White	251 (85.7)	244 (83.3)	232 (79.2)	229 (78.2)
Black	30 (10.2)	41 (14.0)	50 (17.1)	60 (20.5)
Asian	7 (2.4)	4 (1.4)	8 (2.7)	3 (1.0)
Other ^a	5 (1.7)	4 (1.4)	3 (1.0)	1 (0.3)
Ethnicity, n (%)				
Non-Hispanic or Latino	224 (76.5)	197 (67.2)	208 (71.0)	214 (73.0)
Hispanic or Latino	69 (23.5)	96 (32.8)	85 (29.0)	79 (27.0)
rTNSS, mean ± SD ^b	10.1 ± 1.22	10.2 ± 1.25	10.2 ± 1.31	10.3 ± 1.22
iTNSS, mean ± SD ^b	9.2 ± 1.80	9.4 ± 1.70	9.4 ± 1.82	9.6 ± 1.77

GSP301, olopatadine 665 µg/mometasone 25 µg BID; olopatadine, 665 µg BID; mometasone, 25 µg BID.

^aIncludes American Indian or Alaska native, native Hawaiian or other Pacific Islander.

^bFull analysis set.

BID, twice-daily dosing; iTNSS, instantaneous Total Nasal Symptom Score; rTNSS, reflective Total Nasal Symptom Score; SD, standard deviation.

Efficacy

Table 2. LS Mean Difference in Average AM and PM rTNSS and iTNSS Over 14 Days of Treatment

rTNSS				
Treatment Groups (1 vs 2)	n1, n2	LSMD	95% CI	P value
GSP301 vs Placebo	291, 290	-1.09	-1.49, -0.69	<0.001*
GSP301 vs Olopatadine	291, 290	-0.44	-0.84, -0.05	0.028*
GSP301 vs Mometasone	291, 293	-0.47	-0.86, -0.08	0.019*
Olopatadine vs Placebo	290, 290	-0.64	-1.04, -0.25	0.001*
Mometasone vs Placebo	293, 290	-0.62	-1.01, -0.22	0.002*
iTNSS				
GSP301 vs Placebo	291, 290	-0.94	-1.32, -0.56	<0.001*
GSP301 vs Olopatadine	291, 290	-0.41	-0.78, -0.03	0.035*
GSP301 vs Mometasone	291, 293	-0.51	-0.88, -0.13	0.008*
Olopatadine vs Placebo	290, 290	-0.54	-0.92, -0.16	0.005*
Mometasone vs Placebo	293, 290	-0.44	-0.81, -0.06	0.023*

GSP301, olopatadine 665 µg/mometasone 25 µg BID; olopatadine, 665 µg BID; mometasone, 25 µg BID.

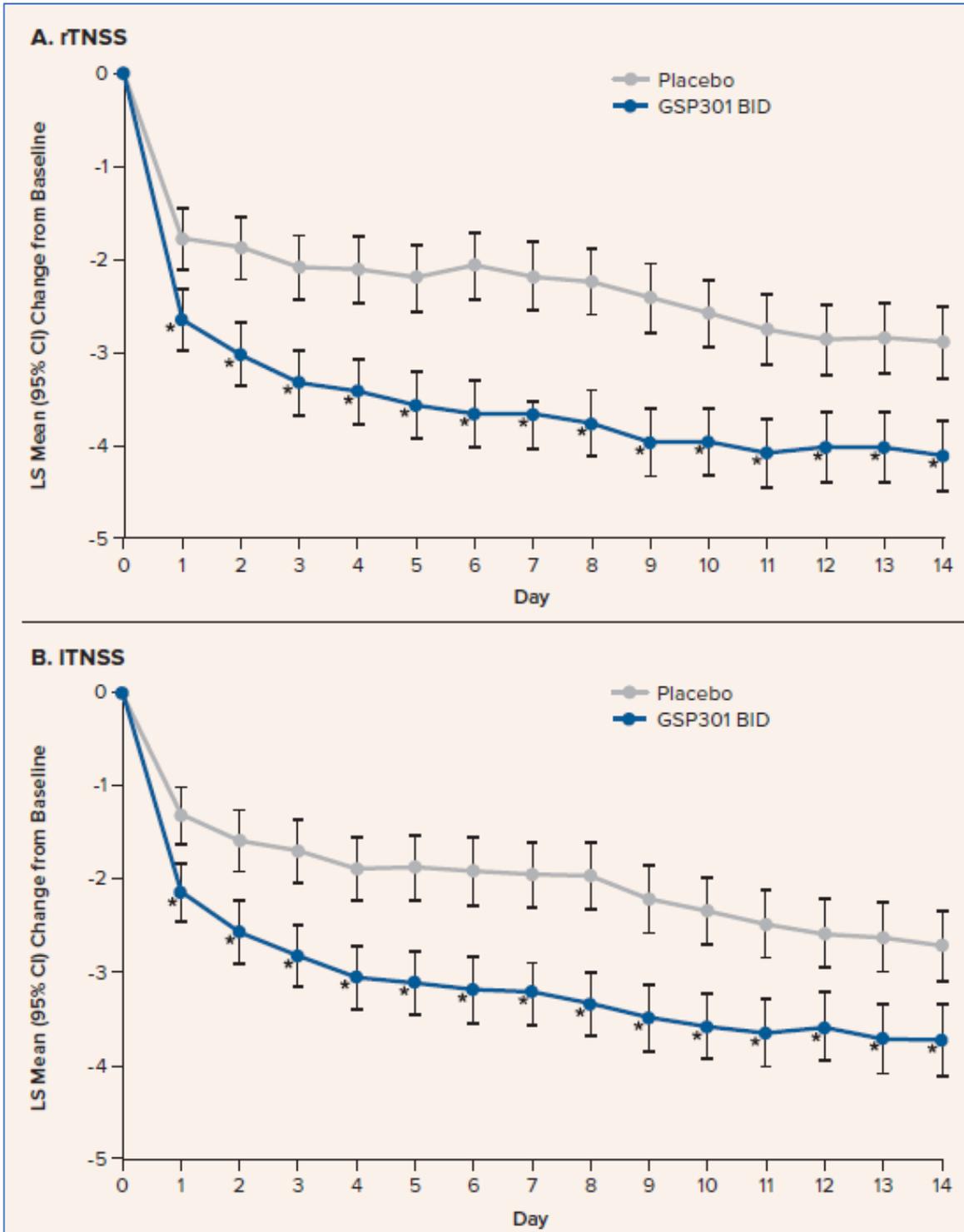
*Indicates significant P values vs treatment group 2.

BID, twice-daily dosing; CI, confidence interval; LSMD, least squares mean difference; iTNSS, instantaneous Total Nasal Symptom Score; rTNSS, reflective Total Nasal Symptom Score.

- GSP301 significantly improved rTNSS and iTNSS vs placebo from baseline to the end of 14-day treatment versus placebo ($P < 0.001$; **Table 2**) and from day 1 and on each subsequent day up to day 14 (**Figure 2**), suggesting sustained symptom improvement
- GSP301 also significantly improved all individual nasal symptoms versus placebo over the 14-day treatment period ($P < 0.001$, all; **Table 3**)

KEY FINDINGS

Figure 2. LS Mean (95% CI) Change from Baseline in Average AM and PM rTNSS (A) and iTNSS (B) With GSP301 vs Placebo Over 14 Days of Treatment



GSP301, olopatadine 665 µg/mometasone 25 µg BID.

* $P < 0.05$ vs placebo.

BID, twice-daily dosing; CI, confidence interval; LS, least squares; iTNSS, instantaneous Total Nasal Symptom Score; rTNSS, reflective Total Nasal Symptom Score.

Table 3. LS Mean Difference in Individual Reflective and Instantaneous Nasal Symptom Scores With GSP301 vs Placebo

Reflective	LSMD (95% CI)	P value
Rhinorrhea	-0.30 (-0.41, -0.19)	<0.001*
Nasal congestion	-0.20 (-0.30, -0.09)	<0.001*
Nasal itching	-0.23 (-0.34, -0.12)	<0.001*
Sneezing	-0.41 (-0.53, -0.29)	<0.001*
Instantaneous	LSMD (95% CI)	P value
Rhinorrhea	-0.29 (-0.39, -0.18)	<0.001*
Nasal congestion	-0.19 (-0.29, -0.09)	<0.001*
Nasal itching	-0.21 (-0.32, -0.10)	<0.001*
Sneezing	-0.29 (-0.41, -0.18)	<0.001*

GSP301, olopatadine 665 µg/mometasone 25 µg BID.

*Indicates significant P values vs placebo.

BID, twice-daily dosing; CI, confidence interval; LSMD, least squares mean difference.

Safety

- The majority of TEAEs were mild or moderate in severity and were not considered related to treatment (Table 4)
 - Only 1 TEAE (dysgeusia) occurred in ≥2% of patients in any treatment group
 - Three patients withdrew due to a TEAE, all in the olopatadine group: bronchitis (n=1), upper respiratory tract infection (n=1), and seizure (n=1)
 - Four patients experienced 8 SAEs (foot fracture, syncope and osteomyelitis [n=1]; diverticulitis, large intestinal obstruction, and large intestinal perforation [n=1]; ischemic stroke [n=1]; peritonsillar abscess [n=1]); none were considered related to study treatment

Table 4. Adverse Events

n, (%)	GSP301 (n=293)	Olopatadine (n=293)	Mometasone (n=293)	Placebo (n=293)
Patients reporting ≥1 TEAE	46 (15.7)	37 (12.6)	28 (9.6)	28 (9.6)
TEAEs (≥2%)				
Dysgeusia	11 (3.8)	2 (0.7)	0 (0)	0 (0)
Patients with a TEAE leading to withdrawal	0 (0)	3 (1.0)	0 (0)	0 (0)
Patients with an SAE	0 (0)	2 (0.7)	1 (0.3)	1 (0.3)
Deaths	0 (0)	0 (0)	0 (0)	0 (0)

GSP301, olopatadine 665 µg/mometasone 25 µg BID; olopatadine, 665 µg BID; mometasone, 25 µg BID.

BID, twice-daily dosing; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- In this study, twice-daily (BID) treatment with GSP301 fixed-dose combination nasal spray resulted in significant, sustained, and clinically meaningful¹ improvements in SAR nasal symptoms compared with placebo and component monotherapies
- GSP301 was well tolerated with similar incidences of AEs compared with placebo or individual monotherapies
- These results demonstrate that GSP301 BID is efficacious and well tolerated for the treatment of nasal symptoms associated with SAR in adult and adolescent patients 12 years of age and older

REFERENCE

1. Barnes ML, et al. *Clin Exp Allergy*. 2010;40(2):242-250.