EFFICACY AND SAFETY OF ONCE-DAILY AND TWICE-DAILY OLOPATADINE/MOMETASONE NASAL SPRAY TREATMENT IN SEASONAL ALLERGIC RHINITIS

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ABSTRACT

Introduction

In patients with allergic rhinitis (AR), intranasal combination treatment with an antihistamine and a corticosteroid may provide improved symptom relief over monotherapy treatment. GSP301 nasal spray is a fixed-dose combination of the antihistamine olopatadine hydrochloride and the corticosteroid mometasone furoate. Efficacy and safety of GSP301 once-daily (QD) or twice-daily (BID) were evaluated in this seasonal AR (SAR) study.

Methods

In this randomized, double-blind, parallel-group study, patients (≥12 years) with SAR were equally randomized to GSP301 BID (olopatadine 665 µg/mometasone 25 µg), GSP301 QD (olopatadine 665 µg/mometasone 50 µg), olopatadine monotherapy (665 µg BID or QD), mometasone monotherapy (25 µg BID or 50 µg QD), or placebo for 14 days. The primary endpoint—mean change from baseline in AM and PM reflective Total Nasal Symptom Score (rTNSS)—was analyzed using ANCOVA. Adverse events (AEs) were also assessed.

Results

A total of 1,111 patients were randomized. GSP301 BID or QD treatment significantly improved rTNSS vs placebo (least squares mean difference [95% CI] GSP301 BID: -1.17 [-1.73, -0.61]; GSP301 QD: -1.11 [-1.67, -0.55]; $P<0.0001$, both). GSP301 BID treatment also showed significant improvement vs olopatadine (-0.49 [-0.98, -0.00]; $P=0.049$) and mometasone (-0.71 [-1.20, -0.22]; $P=0.004$). The percentages of patients reporting treatment-emergent AEs were 10.8%, 9.5%, and 8.2%, with GSP301 BID, GSP301 QD, and placebo.

Conclusion

In this study, GSP301 BID was the optimally efficacious and safe dosage regimen for the treatment of SAR. GSP301 NS BID provided significant and clinically meaningful improvements in SAR symptoms vs placebo and individual monotherapies. GSP301 BID was well tolerated.

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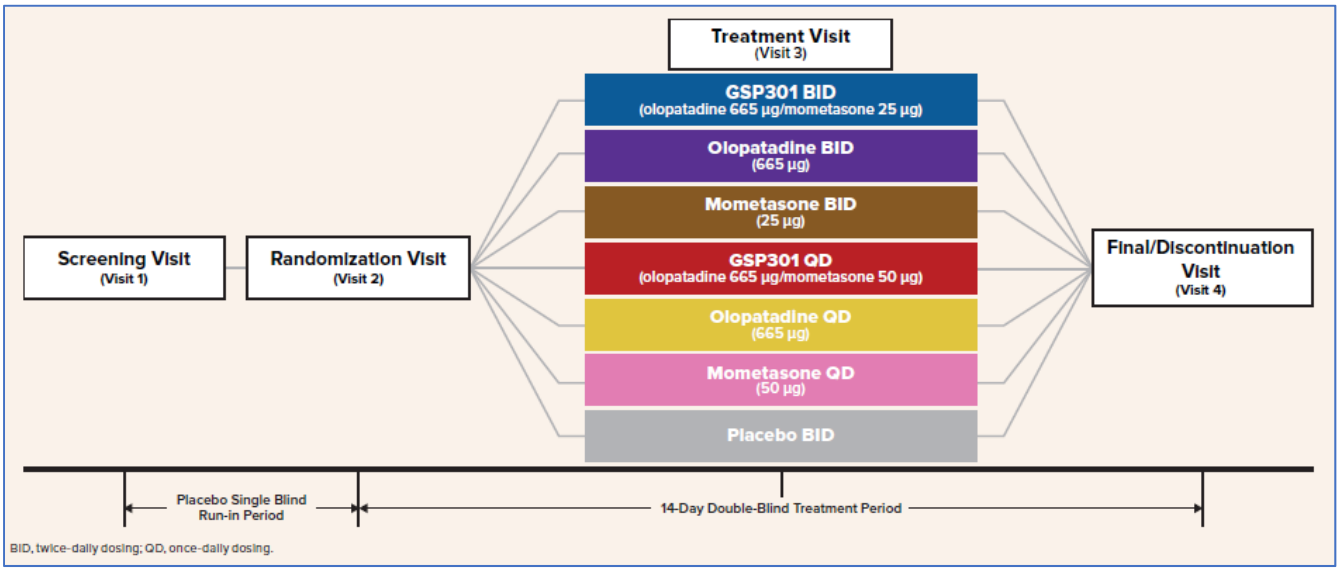
KEY FINDINGS

STUDY DESIGN

- Phase 2, randomized, double-blind, double-dummy, parallel-group study (NCT02318303) conducted during the mountain cedar pollen season (**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
- Safety was monitored via laboratory and physical examinations, ear, nose and throat examinations, vital signs, ECG, and adverse events (AEs)
- A difference of 0.23 units in TNSS was considered clinically meaningful (defined as the minimal clinically important difference)[1]

Figure 1. Study Design



Endpoints

- Primary: mean change from baseline to end of 14-day treatment in patient-reported AM and PM rTNSS for:
  - GSP301 treatment (BID or QD) vs placebo
  - GSP301 treatment (BID or QD) vs olopatadine monotherapy
  - GSP301 treatment (BID or QD) vs mometasone monotherapy
- Additional: change from baseline in AM and PM rTNSS improvements by treatment day and change from baseline in reflective individual nasal symptom scores; and AEs

RESULTS

Patients

- Efficacy analyses were based on the full analysis set (FAS) population, defined as all randomized patients who received ≥1 dose of study drug, and completed ≥1 post-baseline primary efficacy assessment (n=1,110)
- Safety assessments based on the safety analysis set (SAS) consisting of all participants who received ≥1 dose of study drug (n=1,111)
- Demographic and baseline characteristics were comparable among treatment groups (**Table 1**)

KEY FINDINGS

Table 1. Baseline Characteristics

	GSP301 BID (n=157)	Olopatadine BID (n=160)	Mometasone BID (n=159)	GSP301 QD (n=158)	Olopatadine QD (n=158)	Mometasone QD (n=160)	Placebo (n=159)
Age, mean ± SD, y	43.4 ± 14.1	43.5 ± 13.9	44.6 ± 13.7	43.8 ± 13.6	41.9 ± 12.5	44.4 ± 14.3	45.4 ± 15.0
Sex, n (%)							
Male	46 (29.3)	59 (36.9)	63 (39.6)	58 (36.7)	53 (33.5)	45 (28.1)	47 (29.6)
Female	111 (70.7)	101 (63.1)	96 (60.4)	100 (63.3)	105 (66.5)	115 (71.9)	112 (70.4)
Race, n (%)							
White	129 (82.2)	132 (82.5)	126 (79.2)	132 (83.5)	131 (82.9)	127 (79.4)	133 (83.6)
Black	23 (14.6)	24 (15.0)	27 (17.0)	20 (12.7)	26 (16.5)	28 (17.5)	24 (15.1)
Asian	3 (1.9)	3 (1.9)	5 (3.1)	4 (2.5)	1 (0.6)	4 (2.5)	1 (0.6)
Other	2 (1.3)	1 (0.6)	1 (0.6)	2 (1.3)	0 (0)	1 (0.6)	1 (0.6)
Ethnicity, n (%)							
Non-Hispanic or Latino	78 (49.7)	88 (55.0)	93 (58.5)	98 (62.0)	90 (57.0)	99 (61.9)	101 (63.5)
Hispanic or Latino	79 (50.3)	72 (45.0)	66 (41.5)	60 (38.0)	68 (43.0)	61 (38.1)	58 (36.5)
rTNSS, mean ± SD[a]	10.4 ± 1.19	10.3 ± 1.24	10.5 ± 1.13	10.4 ± 1.24	10.3 ± 1.26	10.4 ± 1.30	10.3 ± 1.18

GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 50 µg; Olopatadine BID and QD, 665 µg; Mometasone BID, 25 µg; Mometasone QD, 50 µg.
[a]Full analysis set.
BID, twice-daily dosing; rTNSS, reflective Total Nasal Symptom Score; QD, once-daily dosing; SD, standard deviation.

Efficacy

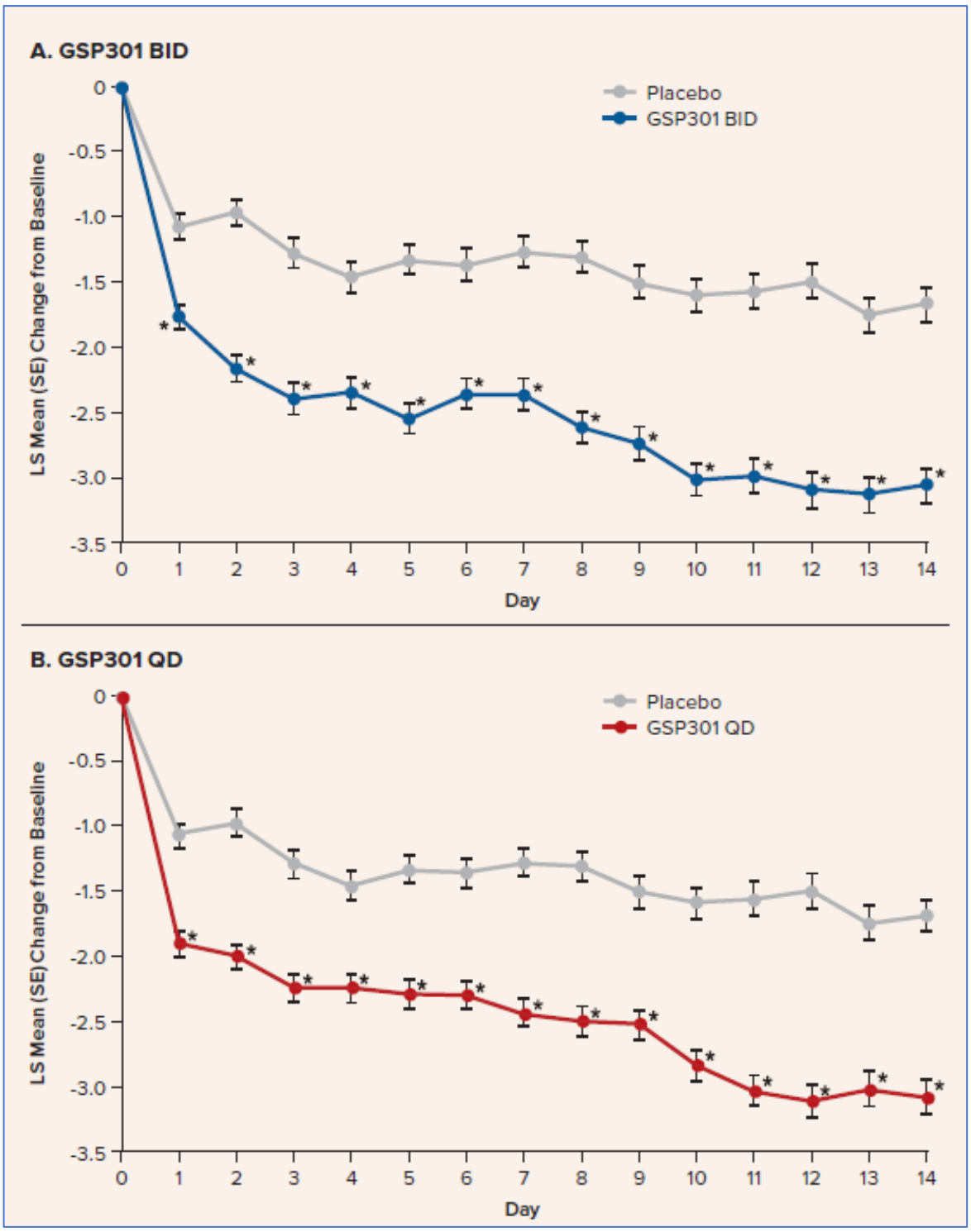
Table 2. LS Mean Difference in Average AM and PM rTNSS Over 14 Days of Treatment

Treatment Groups (1 vs 2)	n1, n2	LSMD	CI	*P* value
GSP301 BID vs Placebo	157, 158	-1.17	-1.73, -0.61[a]	<0.0001*
GSP301 BID vs Olopatadine BID	157, 160	-0.49	-0.98, 0.00[b]	0.049
GSP301 BID vs Mometasone BID	157, 159	-0.71	-1.20, -0.22[b]	0.004*
GSP301 QD vs Placebo	158, 158	-1.11	-1.67, -0.55[a]	<0.0001*
GSP301 QD vs Olopatadine QD	158, 158	-0.77	-1.26, -0.28[b]	0.002*
GSP301 QD vs Mometasone QD	158, 160	-0.36	-0.84, 0.13[b]	0.152

GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 50 µg; Olopatadine BID and QD, 665 µg; Mometasone BID, 25 µg; Mometasone QD, 50 µg.
[a]97.5% CI.
[b]95%CI.
*indicates significant P values vs treatment group 2.
BID, twice-daily dosing; CI, confidence interval; LSMD, least squares mean difference; QD, once-daily; rTNSS, reflective Total Nasal Symptom Score.

- GSP301 BID and QD treatments significantly improved rTNSS vs placebo from baseline to end of treatment (*P*<0.0001; **Table 2**) and on day 1 and on each subsequent day up to day 14 (BID: *P*<0.01 all, **Figure 2A**; QD: *P*<0.01 all, **Figure 2B**) suggesting sustained symptom improvement
- GSP301 BID and QD treatments also significantly improved all individual nasal symptoms versus placebo over the 14-day treatment period (**Table 3**)

Figure 2. LS Mean (SE) Change from Baseline in Average AM and PM rTNSS for GSP301 BID (A) and QD (B) Treatments vs Placebo Over 14 Days of Treatment



GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 50 µg.
*$P<0.05$ vs placebo.
BID, twice-daily dosing; LS, least squares; QD, once-daily dosing; rTNSS, reflective Total Nasal Symptom Score; SE, standard error.

KEY FINDINGS

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

GSP301 BID	LSMD (97.5% CI)	*P* value
Rhinorrhea	-0.27 (-0.42, -0.12)	<0.001*
Nasal congestion	-0.24 (-0.38, -0.99)	<0.001*
Nasal itching	-0.27 (-0.43, -0.11)	<0.001*
Sneezing	-0.39 (-0.57, -0.22)	<0.001*
GSP301 QD		
Rhinorrhea	-0.26 (-0.40, -0.11)	<0.001*
Nasal congestion	-0.22 (-0.37, -0.08)	<0.001*
Nasal itching	-0.26 (-0.42, -0.10)	<0.001*
Sneezing	-0.37 (-0.55, -0.20)	<0.001*

GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 50 µg.
*indicates significant P values vs placebo.
BID, twice-daily dosing; CI, confidence interval; LSMD, least squares mean difference; QD, once-daily dosing.

Safety

- The majority of AEs were mild to moderate in severity and similar across treatment groups; no deaths occurred (**Table 4**)
  - One patient in the GSP301 QD group experienced 2 SAEs (gastritis and gastrointestinal ulcer) that were considered unrelated to treatment

Table 4. Adverse Events

n, (%)	GSP301 BID (n=157)	Olopatadine BID (n=160)	Mometasone BID (n=159)	GSP301 QD (n=158)	Olopatadine QD (n=158)	Mometasone QD (n=160)	Placebo (n=159)
Patients reporting ≥1 TEAE	17 (10.8)	25 (15.6)	10 (6.3)	15 (9.5)	17 (10.8)	15 (9.4)	13 (8.2)
TEAEs (≥2%)							
Headache	0 (0)	1 (0.6)	1 (0.6)	6 (3.8)	1 (0.6)	2 (1.3)	1 (0.6)
Dysgeusia	2 (1.3)	5 (3.1)	0 (0)	2 (1.3)	2 (1.3)	0 (0)	0 (0)
SAEs	0 (0)	0 (0)	0 (0)	1 (0.6)	0 (0)	0 (0)	0 (0)
Deaths	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 50 µg;
Olopatadine BID and QD, 665 µg; Mometasone BID, 25 µg; Mometasone QD, 50 µg.
BID, twice-daily dosing; QD, once-daily dosing; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- In this study, treatment with GSP301 BID and QD dosing regimens resulted in statistically significant and clinically meaningful[1] improvements in nasal symptoms vs placebo, as assessed by patient-reported rTNSS
- GSP301 BID provided significant and clinically meaningful[1] improvements in SAR nasal symptoms compared with either placebo or individual monotherapies
- GSP301 BID and QD treatment regimens were well tolerated, with similar incidences of AEs compared with placebo or individual monotherapies
- Based on these results, GSP301 BID is the optimally efficacious and well tolerated dosage regimen 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.