OLOPATADINE/MOMETASONE COMBINATION NASAL SPRAY EFFECTIVELY IMPROVES SESONAL ALLERGIC RHINITIS NASAL SYMPTOMS AND QUALITY OF LIFE

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ABSTRACT

Introduction

Seasonal allergic rhinitis (SAR) symptoms are troublesome and may contribute to impaired quality of life (QoL). In a randomized, double-blind phase 2 study, an investigational fixed-dose combination of once-daily (QD) or twice-daily (BID) olopatadine hydrochloride/mometasone furoate nasal spray (GSP301) significantly improved average AM and PM reflective Total Nasal Symptom Scores (rTNSS; primary endpoint, presented elsewhere) vs placebo. Additional efficacy and QoL endpoints are reported here.

Methods

Patients with SAR (≥12 years; N=1,111) were equally randomized to GSP301 BID (olopatadine 665 µg/mometasone 25 µg), GSP301 QD (olopatadine 665 µg/mometasone 50 µg), olopatadine (665 µg BID/QD), mometasone (25 µg BID or 50 µg QD), or placebo (GSP301 vehicle) for 14 days. Mean change from baseline in average 12-hour AM and PM instantaneous TNSS (iTNSS), Physician-assessed Nasal Symptom Score (PNSS), and Rhinoconjunctivitis Quality of Life Questionnaire–Standardized Activities [RQLQ(S)] for GSP301 BID and QD vs placebo were analyzed using analysis of covariance (ANCOVA; $P<0.025$ = statistically significant). Adverse events (AEs) were also assessed.

Results

Compared with placebo, GSP301 BID and QD significantly improved iTNSS (least squares mean difference [97.5% CI] GSP301 BID: -1.11 [-1.65, -0.57]; QD: -1.11 [-1.65, -0.57]; $P<0.001$, both) and all individual instantaneous nasal symptoms (BID and QD: $P<0.001$, all). GSP301 BID and QD also significantly improved overall PNSS (BID and QD: $P<0.001$) and overall RQLQ(S) scores (BID: $P<0.001$; QD: $P=0.005$) vs placebo. Treatment-emergent AEs were 10.8%, 9.5%, and 8.2%, for GSP301 BID, QD, and placebo groups, respectively.

Conclusion

GSP301 BID and QD treatments provided statistically significant improvements in both SAR nasal symptoms and patient QoL vs placebo.

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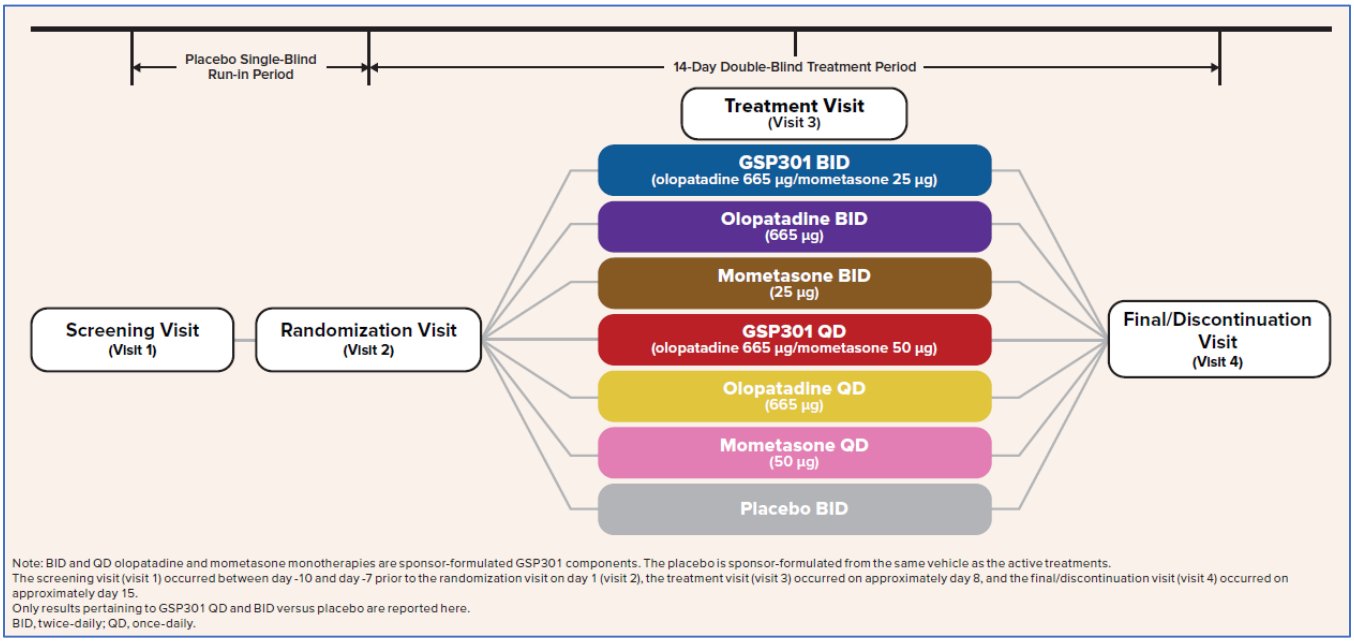
KEY FINDINGS

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 and non-nasal symptoms 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 [MCID])[1]
- A treatment difference of 0.50 units[2] was considered clinically meaningful (defined as MCID)
- For all GSP301 BID and QD versus placebo comparisons, $P<0.025$ = statistically significant; all other treatment comparisons were set at $P<0.05$ (not shown here)

Figure 1. Study Design.



Note: BID and QD olopatadine and mometasone monotherapies are sponsor-formulated GSP301 components. The placebo is sponsor-formulated from the same vehicle as the active treatments.
The screening visit (visit 1) occurred between day -10 and day -7 prior to the randomization visit on day 1 (visit 2), the treatment visit (visit 3) occurred on approximately day 8, and the final/discontinuation visit (visit 4) occurred on approximately day 15.
Only results pertaining to GSP301 QD and BID versus placebo are reported here.
BID, twice-daily; QD, once-daily.

Endpoints

- Patient-reported nasal symptoms were assessed based on mean change from baseline to end of 14-day treatment in average AM and PM 12-hour instantaneous TNSS (iTNSS)
- Physician-assessed nasal symptoms were evaluated based on mean change from baseline to day 15 in overall PNSS and individual symptoms
- Patient-reported QoL was evaluated through mean change from baseline to day 15 in overall RQLQ(S) scores and individual domains
- Treatment-emergent AEs (TEAEs) were also examined
- Only results pertaining to GSP301 QD and BID versus placebo are reported here

KEY FINDINGS

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 symptom and QoL scores were comparable among treatment groups (**Table 1**)

Table 1. Baseline Characteristics

Demographics	GSP301 BID (n=157)	GSP301 QD (n=158)	Placebo (n=159)
Age, mean ± SD, y	43.4 ± 14.1	43.8 ± 13.6	45.4 ± 15.0
Sex, n (%)			
Male	46 (29.3)	58 (36.7)	47 (29.6)
Female	111 (70.7)	100 (63.3)	112 (70.4)
Race, n (%)			
White	129 (82.2)	132 (83.5)	133 (83.6)
Black	23 (14.6)	20 (12.7)	24 (15.1)
Asian	3 (1.9)	4 (2.5)	1 (0.6)
Other	2 (1.3)	2 (1.3)	1 (0.6)
Ethnicity, n (%)			
Non-Hispanic or Latino	78 (49.7)	98 (62.0)	101 (63.5)
Hispanic or Latino	79 (50.3)	60 (38.0)	58 (36.5)
Baseline symptom and QoL scores, mean ± SD	GSP301 BID (n=157)	GSP301 QD (n=158)	Placebo (n=158)
Average AM and PM iTNSS	9.9 ± 1.7	9.8 ± 1.7	9.6 ± 1.7
PNSS	9.6 ± 2.0	9.7 ± 2.0	9.4 ± 2.1
RQLQ(S) score[a]	4.7 ± 0.8	4.7 ± 0.8	4.7 ± 0.8

GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 50 µg; placebo, GSP301 vehicle.
[a] RQLQ population: GSP301 BID n=128; GSP301 QD n=129; placebo n=133.
BID, twice-daily; iTNSS, instantaneous Total Nasal Symptom Score; PNSS, Physician Assessment of Nasal Symptom Scores; QD, once-daily; QoL, quality of life; RQLQ(S), Rhinoconjunctivitis Quality of Life Questionnaire – Standardized Activities; SD, standard deviation.

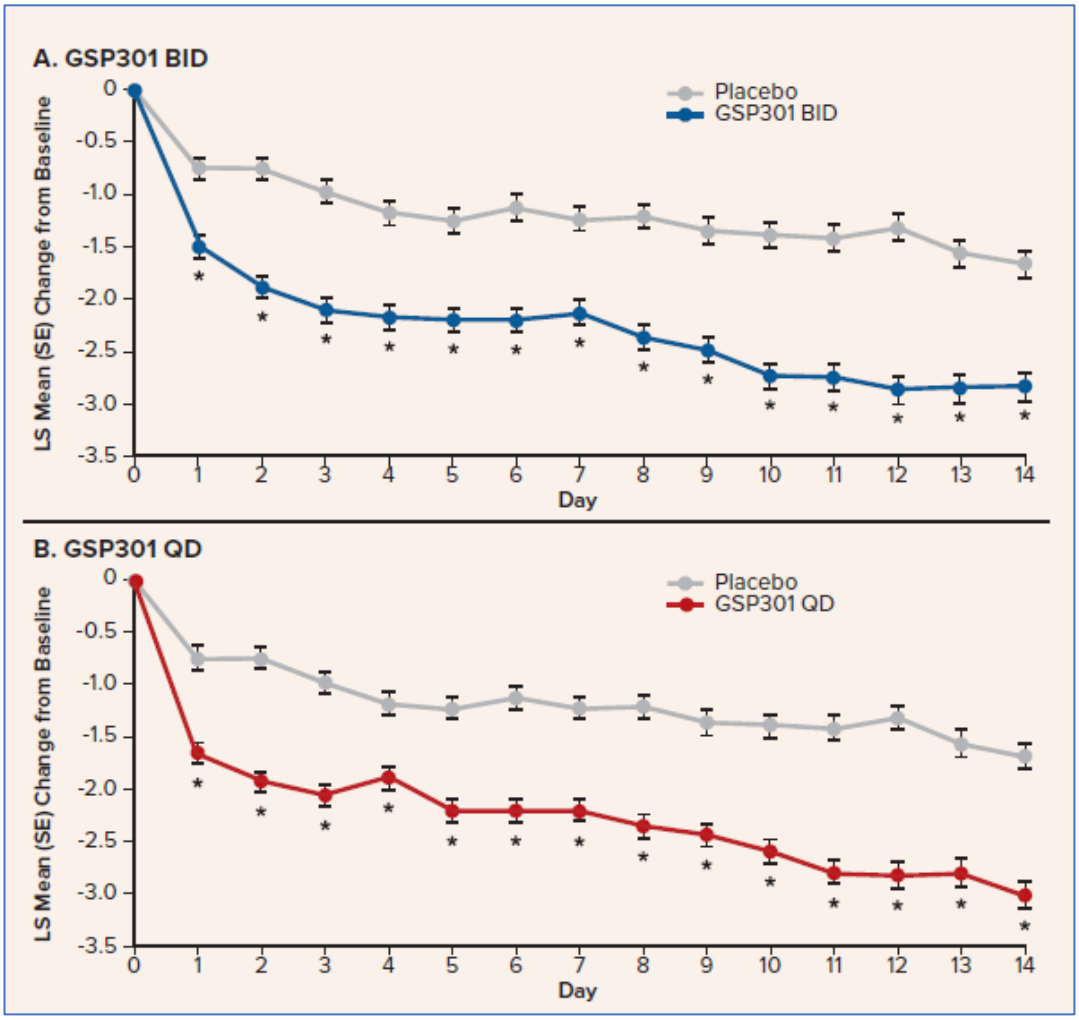
Efficacy

- GSP301 BID and QD treatments demonstrated statistically significant and clinically meaningful improvements in average AM and PM 12-hour iTNSS from baseline to the end of 14-day treatment versus placebo (least squares mean difference [97.5% CI] BID: -1.11 [-1.65, -0.57], P<0.001; QD: -1.11 [-1.65, -0.57], *P*<0.001; **Table 2**)
- GSP301 BID and QD also provided significant and clinically meaningful improvements in iTNSS compared with placebo on day 1 and on each subsequent day up to day 14 (BID: *P*≤0.001 all, **Figure 2A**; QD: *P*≤0.01 all, **Figure 2B**), suggesting sustained nasal symptom improvement
- Additionally, GSP301 BID and QD treatments significantly improved all instantaneous individual nasal symptoms versus placebo over the 14-day treatment period (*P*<0.001, all; **Table 2**)
- Significant improvements in overall PNSS were observed with GSP301 BID and QD versus placebo (*P*≤0.001, both; **Table 3**)
- GSP301 BID also provided significant improvements on all individual symptoms versus placebo (*P*≤0.001, all; **Table 3**)

KEY FINDINGS

- GSP301 QD significantly improved all individual symptoms compared with placebo (P<0.001), with the exception of nasal itching (P=0.081; **Table 3**)
- GSP301 BID and QD provided significant and clinically meaningful improvements in overall RQLQ(S) versus placebo (BID: P<0.001; QD: P=0.002; **Table 4**)
- On the individual domains, both GSP301 BID and QD treatment resulted in significant improvements compared with placebo on all individual domains (BID: P<0.01, all; with the exception of sleep and eye symptoms for GSP301 QD (P=0.045 and P=0.031, respectively; **Table 4**)

Figure 2. Mean Change from Baseline in Average AM and PM 12-hour iTNSS for GSP301 BID (A) and QD (B) Versus Placebo Over 14 Days



GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 50 µg; placebo, GSP301 vehicle.
* Indicates significance (P<0.025) vs placebo.
BID, twice-daily; iTNSS, instantaneous Total Nasal Symptom Score; LS, least squares; QD, once-daily; SE, standard error.

Table 2. Mean Change from Baseline in Instantaneous TNSS and Individual Nasal Symptom Scores With GSP301 Versus Placebo

GSP301 BID (n=157)	LSMD (97.5% CI)	*P* value
Average AM and PM 12-hour iTNSS	-1.11 (-1.65, -0.57)	<0.001*
Individual Symptoms		
Rhinorrhea	-0.27 (-0.42, -0.13)	<0.001*
Nasal congestion	-0.24 (-0.37, -0.10)	<0.001*
Nasal itching	-0.27 (-0.42, -0.12)	<0.001*
Sneezing	-0.33 (-0.50, -0.16)	<0.001*
GSP301 QD (n=158)		
Average AM and PM 12-hour iTNSS	-1.11 (-1.65, -0.57)	<0.001*
Individual Symptoms		
Rhinorrhea	-0.27 (-0.42, -0.13)	<0.001*
Nasal congestion	-0.22 (-0.36, -0.09)	<0.001*
Nasal itching	-0.28 (-0.43, -0.13)	<0.001*
Sneezing	-0.33 (-0.50, -0.17)	<0.001*

GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 25 µg; placebo, GSP301 vehicle.
* Indicates significance (*P*<0.025) vs placebo (n=158).
BID, twice-daily; CI, confidence interval; LSMD, least squares mean difference; iTNSS, instantaneous Total Nasal Symptoms Scores; QD, once-daily; TNSS, Total Nasal Symptoms Scores..

Table 3. Mean Difference in PNSS at Day 15 With GSP301 BID and QD Versus Placebo

GSP301 vs Placebo	n1, n2	LSMD	97.5% CI	*P* value
Overall				
BID	157, 158	-1.48	2.15, -0.81	<0.001*
QD	158, 158	-1.27	-1.94, -0.60	<0.001*
Individual Domains				
Nasal congestion				
BID	157, 158	-0.31	-0.51, -0.11	<0.001*
QD	158, 158	-0.40	-0.60, -0.20	<0.001*
Nasal itching				
BID	157, 158	-0.30	-0.52, -0.09	0.001*
QD	158, 158	-0.16	-0.38, 0.05	0.081
Rhinorrhea				
BID	157, 158	-0.38	-0.58, -0.17	<0.001*
QD	158, 158	-0.36	-0.56, -0.16	<0.001*
Sneezing				
BID	157, 158	-0.49	-0.71, -0.27	<0.001*
QD	158, 158	-0.35	-0.57, -0.13	<0.001*

GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 25 µg; placebo, GSP301 vehicle.
* Indicates statistical significance (*P*<0.025) versus placebo.
Physicians performed ear, nose, and throat examinations and queried patients about nasal symptom severity.[3]
BID, twice-daily; CI, confidence interval; LSMD, least squares mean difference; PNSS, Physician Assessment of Nasal Symptom Scores; QD, once-daily.

Table 4. Mean Difference in RQLQ(S) at Day 15 With GSP301 BID and QD Versus Placebo

GSP301 vs Placebo	n1, n2	LSMD	97.5% CI	*P* value
Overall				
BID	128, 133	-0.60	-0.98, -0.22	<0.001*
QD	129, 133	-0.53	-0.90, -0.15	0.002*
Individual Domains				
Activities				
BID	127, 132	-0.62	-1.02, -0.21	0.001*
QD	129, 132	-0.53	-0.93, -0.13	0.003*
Sleep				
BID	127, 132	-0.54	-0.98, -0.11	0.005*
QD	129, 132	-0.39	-0.82, 0.05	0.045
Non-nasal/Non-eye symptoms				
BID	126, 132	-0.47	-0.87, -0.07	0.009*
QD	129, 132	-0.54	-0.94, -0.14	0.002*
Practical problems				
BID	127, 132	-0.78	-1.21, -0.35	<0.001*
QD	129, 132	-0.67	-1.10, -0.25	<0.001*
Nasal symptoms				
BID	127, 132	-0.84	-1.25, -0.43	<0.001*
QD	129, 132	-0.72	-1.13, -0.31	<0.001*
Eye symptoms				
BID	127, 132	-0.52	-0.94, -0.10	0.006*
QD	129, 132	-0.40	-0.83, 0.02	0.031
Emotional				
BID	127, 132	-0.60	-1.02, -0.18	0.002*
QD	129, 132	-0.50	-0.92, -0.08	0.008*

GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 25 µg; placebo, GSP301 vehicle.
* Indicates statistical significance (*P*<0.025) versus placebo.
The RQLQ(S) consists of 28 questions covering 7 domains: activities, sleep, non-nasal/non-ocular symptoms, practical problems, nasal symptoms, ocular symptoms, and emotional.[4]
BID, twice-daily; CI, confidence interval; FAS, full analysis set; LSMD, least squares mean difference; QD, once-daily; RQLQ(S), Rhinoconjunctivitis Quality of Life Questionnaire – Standardized Activities.

Safety

- The percentage of patients reporting a TEAE in the GSP301 BID and QD groups (BID: 10.8%; n/N: 17/157; QD: 9.5%; 15/158) was similar to placebo (8.2%; 13/159)
- The majority of TEAEs were mild or moderate in severity; 1 patient in the GSP301 QD group experienced 2 serious AEs (gastritis and gastrointestinal ulcer) that were determined to be unrelated to study treatment
- No deaths occurred

CONCLUSIONS

- In this In this phase 2 SAR study, GSP301 fixed-dose combination nasal spray BID and QD treatments provided statistically significant and clinically meaningful[1,2] improvements in nasal symptoms and QoL versus placebo in adolescent and adult patients (12 years of age and older) with SAR as measured by iTNSS and RQLQ(S)
- GSP301 BID and QD treatments also provided statistically significant improvements in physician-assessed nasal symptoms, further supporting the patient-reported outcomes
- Both GSP301 BID and QD were well tolerated, with similar incidences of AEs compared with placebo
- The previously reported primary endpoint (rTNSS) results[5] demonstrate that GSP301 BID is the optimally efficacious and well-tolerated dosage regimen for the treatment of SAR nasal symptoms; the additional efficacy and QoL endpoints presented here further support this

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