OLOPATADINE/MOMETASONE COMBINATION NASAL SPRAY IMPROVES SEASONAL ALLERGIC RHINITIS SYMPTOMS IN A RAGWEED ENVIRONMENTAL EXPOSURE CHAMBER

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ABSTRACT

Introduction

In patients with allergic rhinitis (AR), combining intranasal antihistamines and corticosteroids 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. In this Proof-of-Concept study, efficacy and safety of GSP301 once-daily (QD) or twice-daily (BID) were evaluated in a ragweed pollen Environmental Exposure Chamber (EEC).

Methods

In this randomized, double-blind, double-dummy, parallel-group study, adult patients (18–65 years) with seasonal AR (SAR) were equally randomized to GSP301 BID (olopatadine 665 µg/mometasone 25 µg), GSP301 QD (olopatadine 665 µg/mometasone 50 µg), Dymista® (azelastine 137 µg/fluticasone 50 µg BID), Patanase® (olopatadine 665 µg BID), or placebo (BID). During two clinic visits (baseline and end of 14-day treatment), patients assessed AR symptoms at specified timepoints in an EEC. The primary endpoint—mean change from baseline in instantaneous Total Nasal Symptom Score (iTNSS) for GSP301 BID or QD versus placebo—was analyzed via ANCOVA. Adverse events (AEs) were also assessed.

Results

A total of 180 patients were randomized. Treatment with GSP301 BID or QD significantly improved iTNSS vs placebo after 14 days of treatment (least squares mean difference [95% CI] GSP301 BID: -3.60 [-4.89, -2.30]; QD: -3.05 [-4.35, -1.76]; $P<0.0001$, both). Treatment-emergent AEs occurred in 22.2%, 30.6% and 16.7% of patients in GSP301 BID, GSP301 QD, and placebo groups, respectively.

Conclusion

In an EEC model, treatment with either GSP301 BID or QD provided significant and clinically meaningful improvements in SAR symptoms vs placebo. GSP301 BID and QD were well tolerated.

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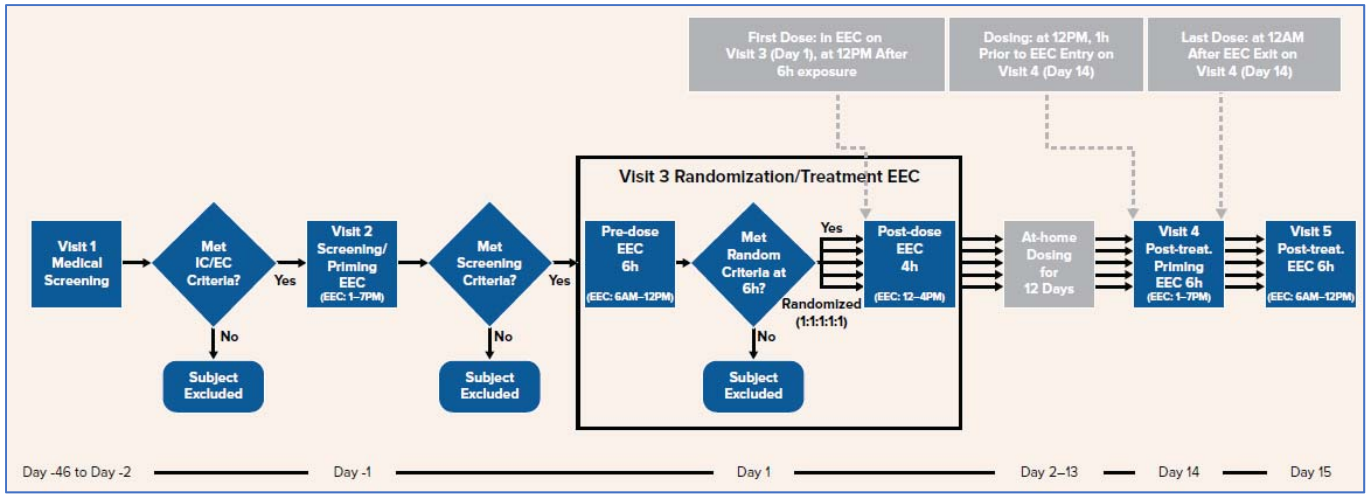
KEY FINDINGS

STUDY DESIGN

- Randomized, double-blind, double-dummy, placebo-controlled, parallel-group proof-of-concept study including adult patients (18 – 65 years) with a clinical history of SAR ≥2 years for ragweed allergen
- Patients were exposed to airborne ragweed pollen (3500 ± 500 particles/m^3) for 6 hours in an EEC at visits 2, 3, 4, and 5 (**Figure 1**)
- At visit 3, patients were equally randomized to 1 of 5 treatments (2 sprays/nostril; **Figure 1**):
  - GSP301 BID (olopatadine 665 µg/mometasone 25 µg)
  - GSP301 QD (olopatadine 665 µg/mometasone 50 µg)
  - Dymista® BID (azelastine 137 µg/fluticasone 50 µg)
  - Patanase® BID (olopatadine 665 µg)
  - Placebo BID (based on the GSP301 formulation)
- Symptoms were assessed at pre-specified timepoints in an electronic diary using the iTNSS
- A treatment difference of 0.23 units in TNSS was considered clinically meaningful (defined as the minimal clinically important difference)[1]

Figure 1. Study Design



During at-home dosing for 12 days, patients self-administered study drug approximately 12 hours apart, based on treatment, without symptom assessment. Visit 2 EEC occurred approximately 24 hours before the first dose of study treatment; Visit 3 EEC was 10 hours, with 6 hours immediately before the first dose of study treatment taken at 12 PM followed by an additional 4 hours after the first dose; Visit 4 EEC occurred approximately 1 hour after the morning (12 PM) dose on Day 14; Visit 5 EEC was approximately 6 hours after the last dose of study treatment taken at 12 AM on Day 14.
EC, exclusion criteria; EEC, environmental exposure chamber; IC, inclusion criteria.

Endpoints

- Primary: mean change from baseline (visit 3) to end of treatment (visit 4) in post-dose iTNSS with GSP301 BID and QD versus placebo
- Secondary: mean change from baseline to end of treatment in post-dose iTNSS with
  - GSP301 BID and QD vs Dymista
  - GSP301 BID and QD vs Patanase
  - Dymista vs placebo
  - Patanase vs placebo
- AEs also assessed

RESULTS

Patients

- A total of 180 patients were randomized
  - Four discontinued: 1 in the GSP301 QD group due to a family emergency and 3 (2 in the Dymista group and 1 in the placebo group) due to procedural non-compliance
- Demographic and baseline characteristics were comparable among treatment groups (**Table 1**)

Table 1. Baseline Characteristics

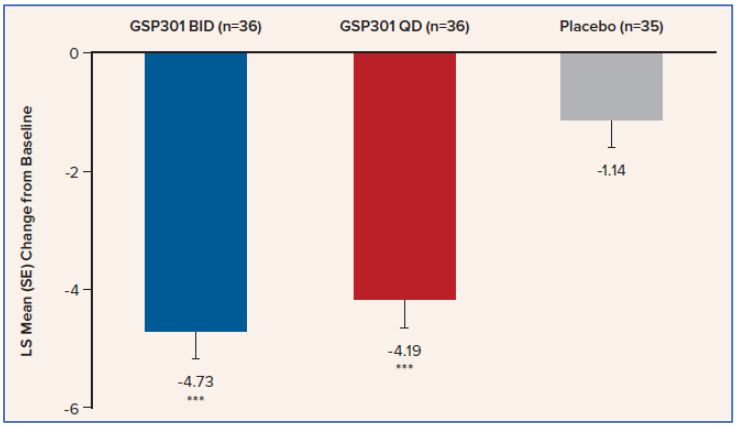
	GSP301 BID (n=36)	GSP301 QD (n=36)	Dymista (n=36)	Patanase (n=36)	Placebo (n=36)
Age, mean ± SD, y	38.3 ± 10.8	44.9 ± 11.8	41.1 ± 10.0	41.6 ± 11.4	42.1 ± 12.5
Sex, n (%)					
Male	22 (61.1)	18 (50.0)	19 (52.8)	16 (44.4)	16 (44.4)
Female	14 (38.9)	18 (50.0)	17 (47.2)	20 (55.6)	20 (55.6)
Weight, mean ± SD, kg	82.0 ± 19.6	81.7 ± 14.2	83.3 ± 17.8	76.2 ± 17.2	76.0 ± 16.5
Race, n (%)					
White	20 (55.6)	14 (38.9)	20 (55.6)	17 (47.2)	18 (50.0)
Black	9 (25.0)	13 (36.1)	13 (36.1)	12 (33.3)	11 (30.6)
Asian	5 (13.9)	8 (22.2)	2 (5.6)	6 (16.7)	7 (19.4)
Other[a]	2 (5.6)	1 (2.8)	1 (2.8)	1 (2.8)	0 (0)
Ethnicity, n (%)					
Non-Hispanic or Latino	32 (88.9)	31 (86.1)	30 (83.3)	33 (91.7)	35 (97.2)
Hispanic or Latino	4 (11.1)	5 (13.9)	6 (16.7)	3 (8.3)	1 (2.8)
iTNSS, mean ± SD[b]	8.07 ± 2.32	8.20 ± 2.05	8.67 ± 2.49	8.27 ± 2.06	7.64 ± 2.18

GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 50 µg; Dymista, azelastine 137 µg/fluticasone 50 µg BID; Patanase, olopatadine 665 µg BID.
[a]Includes patients of mixed race and those that did not identify with the other mentioned race categories.
[b]ITT population.
BID, twice-daily dosing; iTNSS, instantaneous Total Nasal Symptom Score; ITT, intention-to-treat; QD, once-daily dosing; SD, standard deviation.

Efficacy

- Treatment with GSP301 BID or QD showed significant and clinically meaningful improvements in nasal symptoms vs placebo on the primary endpoint (*P*<0.0001, both; **Figure 2**; **Table 2**); this effect was sustained during the entire post-treatment EEC session (**Figure 3**)

Figure 2. iTNSS LS Mean (SE) Change from Baseline (Visit 3) to End of Treatment (Visit 5) for GSP301 BID and QD vs Placebo



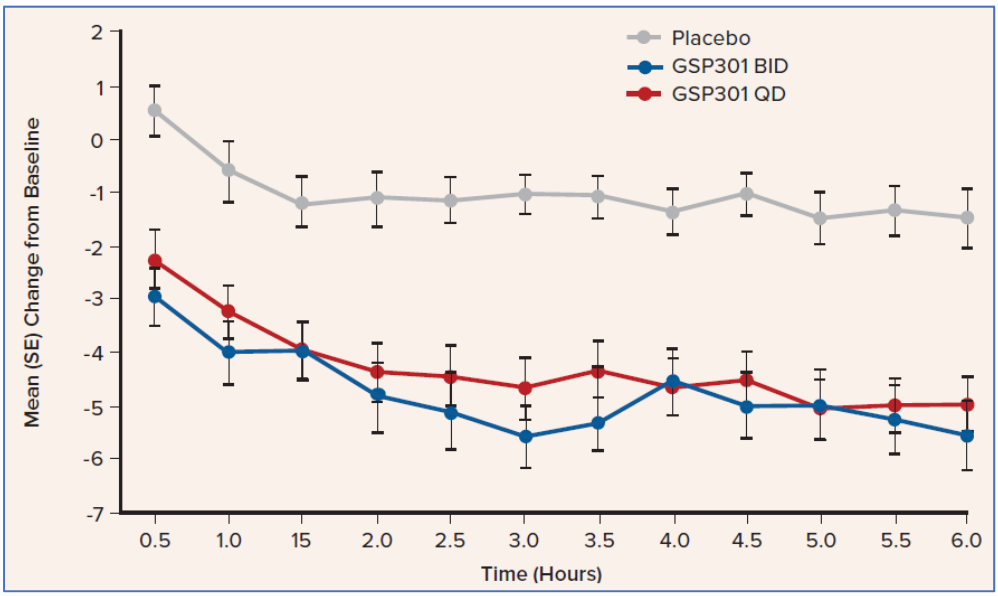
GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 50 µg.
***P<0.0001 vs placebo.
BID, twice-daily dosing; iTNSS, instantaneous Total Nasal Symptom Score; LS, least squares; QD, once-daily dosing; SE, standard error.

Table 2. LS Mean Difference in Average AM and PM iTNSS for GSP301 BID and QD vs Placebo

Treatment Groups (1 vs 2)	n1, n2	LSMD	95% CI	*P* value
GSP301 BID vs Placebo	36, 35	-3.60	-4.89, -2.30	<0.0001*
GSP301 QD vs Placebo	36, 35	-3.05	-4.35, -1.76	<0.0001*

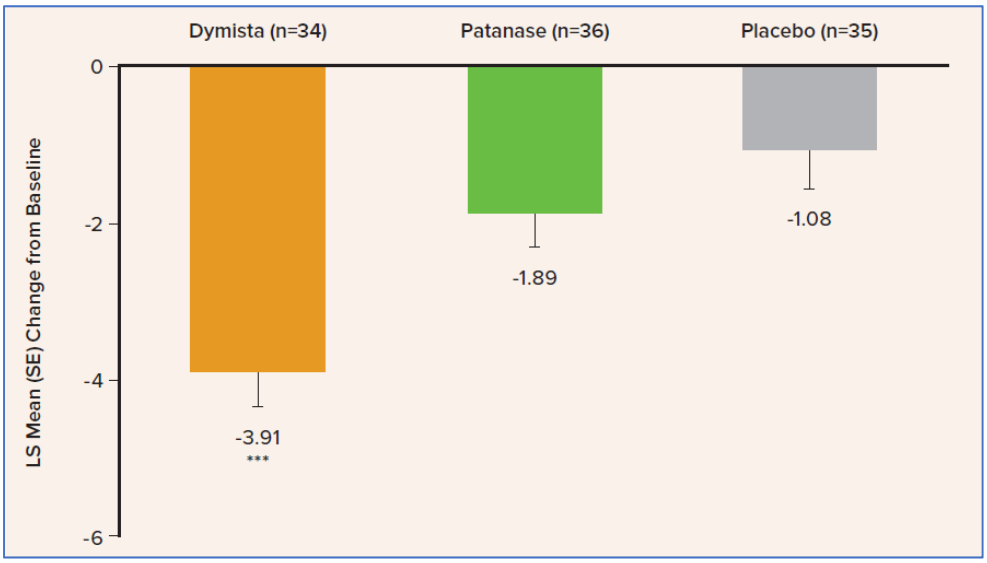
GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 50 µg.
*significant P values vs treatment group 2.
BID, twice-daily dosing; CI, confidence interval; iTNSS, instantaneous Total Nasal Symptom Score;
LSMD, least squares mean difference; QD, once-daily dosing.

Figure 3. iTNSS Mean (SE) Change from Baseline (Visit 3) to End of Treatment (Visit 5) for GSP301 BID and QD vs Placebo



GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 50 µg.
BID, twice-daily dosing; iTNSS, instantaneous Total Nasal Symptom Score; QD, once-daily dosing; SE, standard error.

Figure 4. iTNSS LS Mean (SE) Change from Baseline (Visit 3) to End of Treatment (Visit 5) for Dymista and Patanase vs Placebo



Dymista, azelastine 137 µg/fluticasone 50 µg BID; Patanase, olopatadine 665 µg BID.
****P*<0.0001 vs placebo.
BID, twice-daily dosing; iTNSS, instantaneous Total Nasal Symptom Score; ITT, intention-to-treat; LS, least squares;
SE, standard error.

Table 3. LS Mean Difference in Average AM and PM iTNSS for Dymista and Patanase vs Placebo

Treatment Groups (1 vs 2)	n1, n2	LSMD	95% CI	*P* value
Dymista vs Placebo	34, 35	-2.83	-4.05, -1.61	<0.0001*
Patanase vs Placebo	36, 35	-0.81	-2.00, 0.38	0.179

Dymista, azelastine 137 µg/fluticasone 50 µg BID; Patanase, olopatadine 665 µg BID.
*significant P values vs treatment group 2.
BID, twice-daily dosing; CI, confidence interval; iTNSS, instantaneous Total Nasal Symptom Score; LSMD, least squares mean difference.

- GSP301 BID and QD showed significant and clinically meaningful improvements in iTNSS vs Patanase (LSMD [95% CI] GSP301 BID: -2.94 [-4.23, -1.64], *P*<0.0001; QD: -2.39 [-3.69, -1.10], *P*=0.0004; figure not shown)
- Clinically meaningful numerical improvements in iTNSS with GSP301 BID and QD were observed compared with Dymista, but these did not reach statistical significance (GSP301 BID: -1.09 [-2.46, 0.28], *P*=0.118; QD: -0.53 [-1.90, 0.83], *P*=0.441; figure not shown)

Safety

- The percentage of patients reporting ≥1 treatment emergent AE (TEAE) was generally comparable among treatment groups with a slightly greater percentage in the GSP301 QD group (**Table 4**)
- All TEAEs were mild to moderate; no patients discontinued due to TEAEs and no serious adverse events (SAEs) or deaths were reported

Table 4. Adverse Events

n, (%)	GSP301 BID (n=36)	GSP301 QD (n=36)	Dymista (n=36)	Patanase (n=36)	Placebo (n=36)
Patients reporting ≥1 TEAE	8 (22.2)	11 (30.6)	9 (25.0)	8 (22.2)	6 (16.7)
TEAEs (≥2%)					
Headache	4 (11.1)	6 (16.7)	3 (8.3)	4 (11.1)	3 (8.3)
Dysgeusia	2 (5.6)	1 (2.8)	1 (2.8)	1 (2.8)	0 (0)
Epistaxis	0 (0)	0 (0)	2 (5.6)	2 (5.6)	0 (0)
Rash	0 (0)	0 (0)	0 (0)	2 (5.6)	0 (0)
Treatment-related TEAEs	7 (19.4)	5 (13.9)	5 (13.9)	6 (16.7)	3 (8.3)
TEAEs leading to withdrawal	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
SAEs	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Deaths	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; Dymista, azelastine 137 µg/fluticasone 50 µg BID; Patanase, olopatadine 665 µg BID.
BID, twice-daily; QD, once-daily; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- In an EEC model, treatment with either GSP301 BID or QD provided significant and clinically meaningful[1] SAR nasal symptom improvement versus placebo
- Both GSP301 treatment regimens (BID and QD) were well tolerated with only mild to moderate AEs reported

REFERENCE

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