SEASONAL ALLERGIC RHINITIS NASAL SYMPTOMS AND QUALITY OF LIFE WITH OLOPATADINE/MOMETASONE COMBINATION NASAL SPRAY

GARY N. GROSS[1]; GARY BERMAN[2]; NIRAN J. AMAR[3]; CYNTHIA F. CARACTA[4]; SUDEESH K. TANTRY[4]

[1]PHARMACEUTICAL RESEARCH & CONSULTING INC, DALLAS, TX, US; [2]CLINICAL RESEARCH INSTITUTE, INC, MINNEAPOLIS, MN, US; [3]ALLERGY ASTHMA RESEARCH INSTITUTE, WACO, TX, US; [4]GLENMARK PHARMACEUTICALS INC, PARAMUS, NJ, US

ABSTRACT

Introduction

Seasonal allergic rhinitis (SAR) symptoms often impair quality of life (QoL). In two randomized, double-blind phase 3 SAR studies, twice-daily GSP301 nasal spray, an investigational fixed-dose combination of olopatadine hydrochloride/mometasone furoate, significantly improved reflective and instantaneous Total Nasal Symptom Scores (rTNSS, primary endpoint; iTNSS, secondary endpoint) vs placebo (presented elsewhere). Results of additional endpoints comparing the efficacy and QoL of GSP301 vs placebo are reported here.

Methods

In Study 1 (NCT02631551; N=1,180) and Study 2 (NCT02870205; N=1,176), patients with SAR (≥12 years) 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 (GSP301 vehicle) for 14 days. Mean changes from baseline in Physician-assessed Nasal Symptom Score (PNSS) and Rhinoconjunctivitis Quality of Life Questionnaire–Standardized Activities [RQLQ(S)] for GSP301 vs placebo were analyzed using mixed-effect model repeated measures (P<0.05 = statistically significant). Adverse events (AEs) were also assessed.

Results

GSP301 significantly improved PNSS vs placebo in Study 1 (least squares mean difference [95% CI]: -0.82 [-1.26, -0.38], P<0.001) and Study 2 (-1.30 [-1.75, -0.85], P<0.001), with significant improvements in each individual symptom vs placebo in both studies (P<0.05, all). GSP301 also significantly improved overall RQLQ(S) scores (Study 1: -0.43 [-0.64, -0.21], P<0.001; Study 2: -0.45 [-0.68, -0.22], P<0.001). Treatment-emergent AE rates in studies 1 and 2 were 12.9% and 15.6% with GSP301 and 9.4% and 9.5% with placebo, respectively.

Conclusions

In two phase 3 SAR studies, twice-daily GSP301 treatment provided significant improvements in nasal symptoms and QoL vs placebo and was well tolerated.

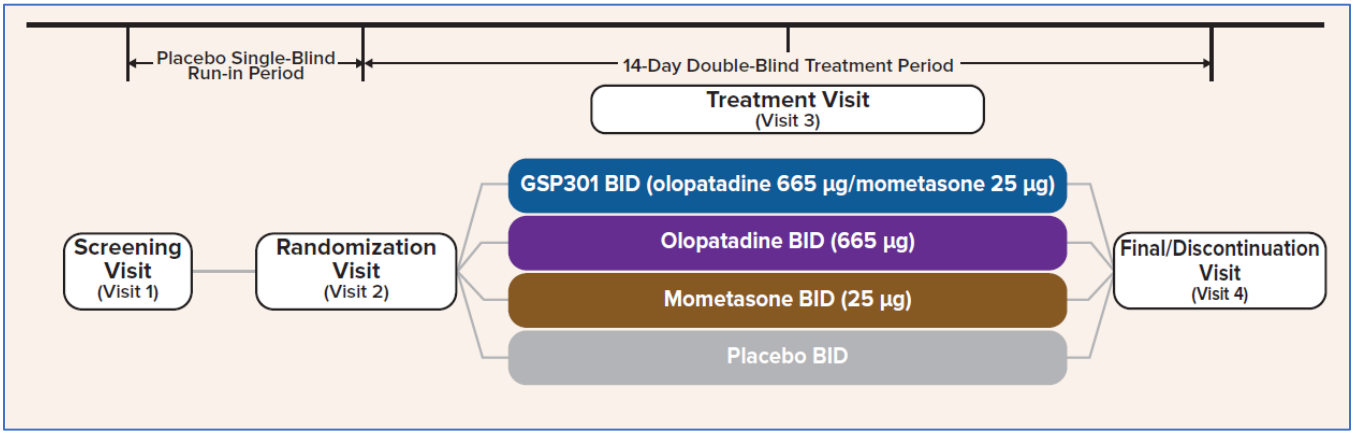
PRESENTED AT THE AMERICAN COLLEGE OF ALLERGY, ASTHMA, AND IMMUNOLOGY ANNUAL MEETING
November 15-19, 2018 I SEATTLE, WA

KEY FINDINGS

STUDY DESIGN

- Two similarly designed double-blind, randomized, parallel-group studies (Study 1 [NCT02631551]; Study 2 [NCT02870205]) were conducted during the Spring (Study 1) and Fall/mountain cedar (Study 2) pollen seasons in patients with SAR (**Figure 1**)
- 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
- Nasal symptoms of congestion, itching, rhinorrhea, and sneezing were assessed using the Physician Assessment of Nasal Symptom Score (PNSS)[1] at visits 2 and 4
- The validated Rhinoconjunctivitis Quality of Life Questionnaire – Standardized Activities [RQLQ(S)][2] was self-administered during visits 2 and 4
  - A treatment difference of 0.50 units on the RQLQ(S) was considered clinically meaningful, defined as the minimal clinically important difference (MCID)[3]

Figure 1. Study Design



GSP301, olopatadine 665 µg/mometasone 25 µg BID; olopatadine, 665 µg BID; mometasone, 25 µg BID.
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. 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 versus placebo are reported here.
BID, twice-daily.

Endpoints

- Physician-assessed nasal symptoms were analyzed based on mean change from baseline to day 15 in overall PNSS and individual symptoms
- Patient-reported QoL was analyzed through mean change from baseline to day 15 in overall RQLQ(S) scores and individual domains
- Treatment-emergent AEs (TEAEs) were also evaluated
- Only results pertaining to GSP301 and placebo are reported here
- 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—and safety results for both trials have been reported elsewhere[4,5]

RESULTS

Patients

- A total of 1,180 and 1,176 patients were randomized in Studies 1 and 2, respectively
- Demographics and baseline symptom and QoL scores were similar across the treatment groups (**Table 1**)
- Patients were predominantly female and white, with mean ages ranging from 39.4 to 39.9 years (**Table 1**)

Table 1. Baseline Characteristics

	Study 1		Study 2	
Demographics	GSP301 (n=302)	Placebo (n=287)	GSP301 (n=293)	Placebo (n=293)
Age, mean ± SD, y	39.5 ± 15.4	39.4 ± 14.8	39.9 ± 14.9	39.6 ± 14.9
Sex, n (%)				
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)
Race, n (%)				
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[a]	3 (1.0)	1 (0.3)	5 (1.7)	1 (0.3)
Ethnicity, n (%)				
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)
Baseline symptom/ QoL scores, mean ± SD	GSP301 (n=299)	Placebo (n=283)	GSP301 (n=292)	Placebo (n=293)
PNSS	9.6 ± 2.1	9.6 ± 1.9	9.2 ± 2.1	9.6 ± 1.8
RQLQ(S) score	4.0 ± 1.1	3.9 ± 1.2	4.0 ± 1.2	4.0 ± 1.2

GSP301, olopatadine 665 µg/mometasone 25 µg BID; placebo, GSP301 vehicle.
[a] Includes American Indian or Alaska native, native Hawaiian or other Pacific Islander.
BID, twice-daily; PNSS, Physician Assessment of Nasal Symptom Scores; QoL, quality of life; RQLQ(S), Rhinoconjunctivitis Quality of Life Questionnaire – Standardized Activities; SD, standard deviation.

Efficacy

- GSP301 demonstrated statistically significant improvements on PNSS versus placebo in Study 1 and Study 2 ($P<0.001$, both), with significant improvements in each of the 4 individual symptoms versus placebo in both studies ($P<0.05$, all; **Table 2**)
- In each study, GSP301 significantly improved overall RQLQ(S) scores compared with placebo ($P<0.001$, both); the MCID of 0.50 units, however, was not met for the overall score in either study (**Table 3**)
- Significant improvements on all individual RQLQ(S) domains were reported for GSP301 versus placebo in Study 1 ($P<0.05$, all); in Study 2, GSP301 provided significant improvements on 5 of 7 individual domains (**Table 3**)

Table 2. Mean Difference in PNSS at Day 15 With GSP301 Versus Placebo

GSP301 vs Placebo	n1, n2	LSMD	95% CI	*P* value
Overall				
Study 1	299, 279	-0.82	-1.26, -0.38	<0.001*
Study 2	292, 290	-1.30	-1.75, -0.85	<0.001*
Individual Domains				
Nasal congestion				
Study 1	299, 279	-0.18	-0.31, -0.05	0.007*
Study 2	292, 290	-0.29	-0.43, -0.16	<0.001*
Nasal itching				
Study 1	299, 279	-0.30	-0.44, -0.15	<0.001*
Study 2	292, 290	-0.26	-0.41, -0.11	<0.001*
Rhinorrhea				
Study 1	299, 279	-0.16	-0.29, -0.03	0.016*
Study 2	292, 290	-0.35	-0.49, -0.21	<0.001*
Sneezing				
Study 1	299, 279	-0.18	-0.32, -0.04	0.010*
Study 2	292, 290	-0.40	-0.54, -0.26	<0.001*

GSP301, olopatadine 665 µg/mometasone 25 µg BID; placebo, GSP301 vehicle.
* Indicates statistical significance ($P<0.05$) versus placebo.
BID, twice-daily; CI, confidence interval; LSMD, least squares mean difference; PNSS, Physician Assessment of Nasal Symptom Scores.

Table 3. Mean Difference in RQLQ(S) at Day 15 With GSP301 Versus Placebo

GSP301 vs Placebo	n1, n2	LSMD	95% CI	*P* value
Overall				
Study 1	298, 279	-0.43	-0.64, -0.21	<0.001*
Study 2	283, 280	-0.45	-0.68, -0.22	<0.001*
Individual Domains				
Activities				
Study 1	298, 279	-0.53	-0.77, -0.29	<0.001*
Study 2	291, 289	-0.49	-0.74, -0.24	<0.001*
Sleep				
Study 1	298, 279	-0.36	-0.61, -0.11	0.004*
Study 2	292, 290	-0.34	-0.60, -0.09	0.009*
Non-nasal/Non-ocular symptoms				
Study 1	298, 279	-0.28	-0.50, -0.05	0.016*
Study 2	287, 282	-0.28	-0.51, -0.04	0.023*
Practical problems				
Study 1	298, 279	-0.46	-0.71, -0.21	<0.001*
Study 2	291, 290	0.33	-0.53, 1.18	0.455
Nasal symptoms				
Study 1	298, 279	-0.61	-0.84, -0.37	<0.001*
Study 2	290, 289	-0.68	-0.93, -0.43	<0.001*
Ocular symptoms				
Study 1	298, 279	-0.47	-0.71, -0.23	<0.001*
Study 2	292, 290	-0.44	-0.70, -0.18	0.001*
Emotional				
Study 1	298, 279	-0.39	-0.63, -0.16	0.001*
Study 2	292, 290	0.10	-0.50, 0.71	0.738

GSP301, olopatadine 665 µg/mometasone 25 µg BID; placebo, GSP301 vehicle.
* Indicates statistical significance ($P<0.05$) versus placebo.
BID, twice-daily; CI, confidence interval; LSMD, least squares mean difference; RQLQ(S), Rhinoconjunctivitis Quality of Life Questionnaire – Standardized Activities.

KEY FINDINGS

Safety

- In both studies, a greater percentage of GSP301-treated patients reported a TEAE than placebo-treated patients:
  - Study 1: GSP301 12.9% (n/N: 39/302); placebo 9.4% (27/287)
  - Study 2: GSP301 15.6% (46/294); placebo 9.5% (28/294)
- Most TEAEs were mild or moderate in severity and were not considered related to treatment; 1 placebo-treated patient in Study 1 discontinued due to a TEAE
- Two patients had serious AEs: 1 treated with GSP301 in Study 1 (spontaneous abortion) and 1 treated with placebo in Study 2 (foot fracture, syncope, and osteomyelitis)
- No deaths occurred in either study

CONCLUSIONS

- In two replicate phase 3 SAR studies, twice-daily GSP301 treatment provided statistically significant improvements in nasal symptoms versus placebo as measured by PNSS
- Treatment with GSP301 also resulted in statistically significant QoL improvements compared with placebo
- GSP301 was well tolerated with similar incidences of AE versus placebo
- Overall, these results demonstrate that GSP301 is efficacious and well tolerated for the treatment of nasal symptoms associated with SAR in adolescent and adult patients 12 years of age and older

REFERENCES

1. Kim K, et al. *Pediatric Asthma, Allergy & Immunology*. 2007;20(4):229-242.10.
2. Juniper EF, et al. *Clin Exp Allergy*. 1991;21(1):77-83.
3. Juniper EF, et al. *J Allergy Clin Immunol*. 1996;98(4):843-845.
4. Ratner P, et al. 2017. Poster presented at the American College of Allergy, Asthma, and Immunology; October 26-30; Boston, MA.
5. Hampel F, et al. 2018. Poster presented at the American Academy of Allergy, Asthma & Immunology/World Allergy Congress Joint Congress; March 2-5; Orlando, FL.