QUALITY OF LIFE IMPROVEMENTS FOLLOWING TREATMENT WITH OLOPATADINE/MOMETASONE COMBINATION NASAL SPRAY IN PATIENTS WITH SEASONAL ALLERGIC RHINITIS: A POOLED ANALYSIS

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ABSTRACT

Rationale

Seasonal allergic rhinitis (SAR) symptoms are troublesome and often impair quality of life (QoL). Demonstrated efficacy, safety and QoL of GSP301, an investigational fixed-dose combination nasal spray containing olopatadine hydrochloride (antihistamine) and mometasone furoate (corticosteroid), have been reported previously. Pooled QoL analyses from 3 SAR studies conducted across different pollen seasons are presented here.

Methods

Twice-daily GSP301 treatment results from double-blind, randomized, placebo-controlled 14-day studies (NCT02318303, NCT02631551, NCT02870205; N=2,971) were pooled. SAR patients (12–65 years old) were equally randomized to twice-daily GSP301 (olopatadine 665 µg/mometasone 25 µg), olopatadine (665 µg), mometasone (25 µg), or placebo. Results from once-daily treatments, evaluated only in NCT02318303, are not shown here. Mean change from baseline to day 15 in overall Rhinoconjunctivitis Quality of Life Questionnaire–Standardized Activities [RQLQ(S)] score was analyzed using ANCOVA (P<0.05=statistically significant). Individual QoL domains were also assessed.

Results

GSP301 demonstrated statistically significant improvements in overall RQLQ(S) scores vs placebo (least squares mean difference [95% CI]: -0.48 [-0.67, -0.30], P<0.001). GSP301 also provided statistically significant improvements vs placebo in each individual domain: activities (-0.55 [-0.75, -0.35], P<0.001); emotional (-0.49 [-0.69, -0.29], P<0.001); eye symptoms (-0.48 [-0.68, -0.27], P<0.001); nasal symptoms (-0.69 [-0.89, -0.49], P<0.001); non-nose/eye symptoms (-0.33 [-0.51, -0.14], P<0.001); practical problems (-0.62 [-0.83, -0.41], P<0.001); and sleep (-0.40 [-0.60, -0.19], P<0.001). Treatment-emergent adverse events were low and comparable across treatments (reported elsewhere).

Conclusions

In a pooled analysis of SAR studies conducted with different seasonal allergens, GSP301 treatment provided statistically significant improvements in QoL vs placebo and was well tolerated.

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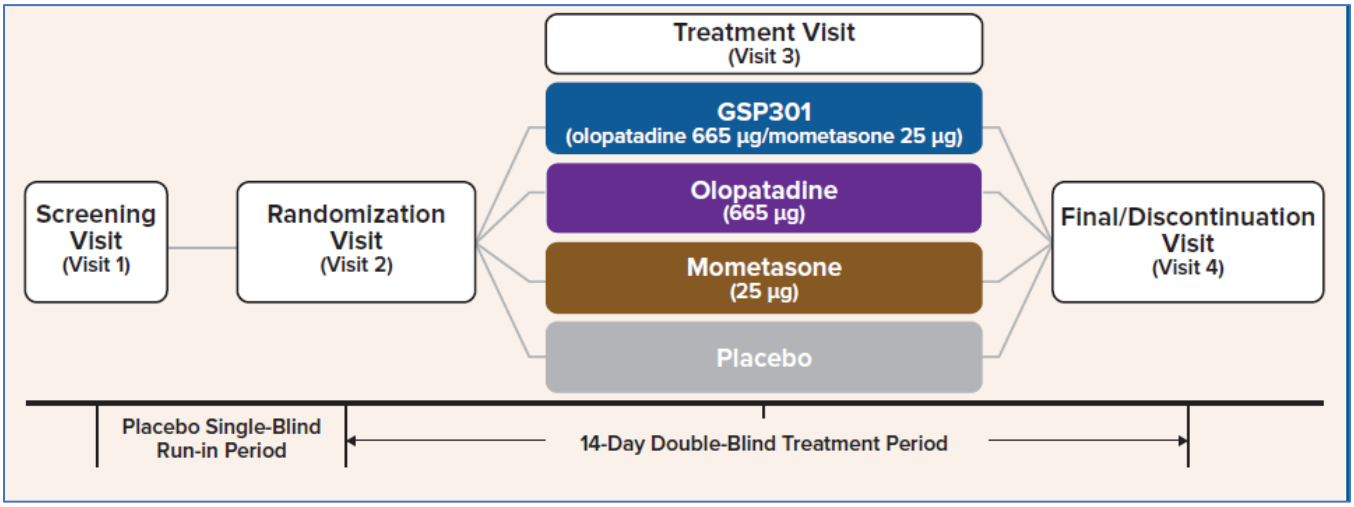
KEY FINDINGS

STUDY DESIGN

- Efficacy results were pooled from 3 randomized, double-blind, placebo-controlled (RDBPC), 14-day SAR studies: Study 1 (NCT02318303; phase 2) and Studies 2 and 3 (NCT02631551 and NCT02870205; phase 3 replicate studies) conducted with different seasonal allergens: mountain cedar (Study 1), spring allergens (Study 2), or fall/mountain cedar (Study 3)
- Each RDBPC study consisted of two periods: a placebo run-in period (7 to 10 days from screening to randomization) and a treatment period (15 to 17 days from randomization to the final treatment visit) (**Figure 1**)
- Safety results were pooled from the 3 RDBPC studies (above) plus a 14-day double-blind, randomized, double-dummy proof-of-concept study (Study 4; NCT03444506) conducted in an environmental exposure chamber (EEC)
- In all four studies, patients self-administered study medication and, twice daily, self-assessed reflective and instantaneous nasal symptoms (nasal congestion, itchy nose, rhinorrhea, and sneezing) and ocular symptoms (itching/burning, tearing/watering, and redness of eyes) in a symptom diary
- Efficacy procedures in Study 4 differed from the RDBPC studies (EEC vs natural allergen exposure design) but treatment exposure time was the same (14 days); thus, only the safety data from Study 4 were included in the pooled analysis presented here (efficacy data previously published[1])

Figure 1. Study Design: Pooled Efficacy Data (Studies 1, 2, and 3)

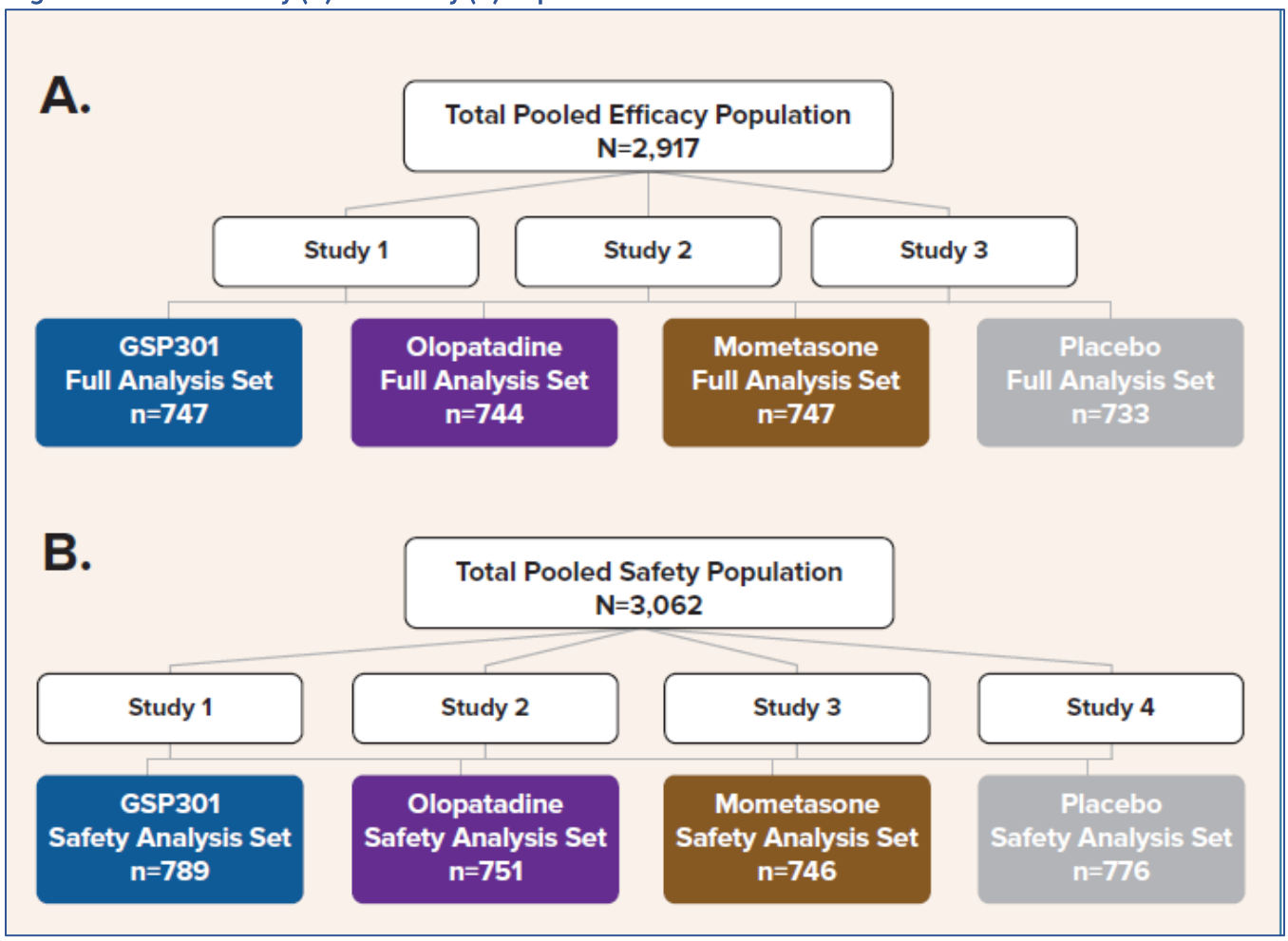


All treatments were self-administered as two sprays per nostril twice daily; additional treatments dosed once daily (Study 1) were not included in the pooled analysis and are not shown here (see Methods for details).
See Methods for Study 4 design (not shown here); only safety data were included in the pooled analysis.

Endpoints

- Pooled QoL analyses (Studies 1, 2, and 3):
  - Mean change from baseline to day 15 (visit 4) in overall Rhinoconjunctivitis Quality of Life Questionnaire – Standardized Activities [RQLQ(S)] and individual domains
  - The validated RQLQ(S) has 28 questions in 7 domains (activities, sleep, non-nose/eye symptoms, practical problems, nasal symptoms, eye symptoms, and emotional)[2]
  - A treatment difference of 0.50 units in overall RQLQ(S) was considered clinically meaningful (defined as the minimal clinically important difference [MCID])[3]
- Pooled safety analysis (Studies 1, 2, 3 and 4):
  - Safety was monitored via adverse events (AEs), laboratory assessments, vital signs, physical examinations, ear, nose and throat examinations, and electrocardiograms
- The pooled analysis of the primary and secondary endpoints—mean change from baseline to the end of treatment in patient-reported AM and PM 12-hour rTNSS and iTNSS, respectively—and detailed safety outcomes have been reported in the TNSS poster
- Only data pertaining to twice-daily GSP301 and placebo treatments are reported here

Figure 2. Pooled Efficacy (A) and Safety (B) Populations



GSP301, olopatadine 665 µg/mometasone 25 µg; olopatadine, 665 µg; mometasone, 25 µg; placebo, GSP301 vehicle.
Note: In Study 1, only patients aged 18 years of age and older were included in the RQLQ(S) analysis. Patients aged 12-17 years were not included.

RESULTS

Patients

- A total of 2,971 patients were included in the pooled efficacy analysis (FAS; **Figure 2A**)
- Most patients were female with a mean age ranging from 40.2 to 40.5 years and moderate to severe symptoms (**Table 1**)
- Demographic characteristics and baseline QoL scores (FAS) were similar across the treatment groups (**Table 1**)

Table 1. Demographics and Baseline Symptom Scores (FAS) – Pooled Analysis

Demographics	GSP301 (n=747)	Placebo (n=733)
Age, mean ± SD, y	40.2 ± 15.0	40.5 ± 15.1
Sex, n (%)		
Female	512 (68.5)	466 (63.6)
Male	235 (31.5)	267 (36.4)
Race, n (%)		
White	617 (82.6)	590 (80.5)
Black	108 (14.5)	129 (17.6)
Other[a]	22 (2.9)	14 (1.9)
Ethnicity, n (%)		
Non-Hispanic or Latino	529 (70.8)	531 (72.4)
Hispanic or Latino	218 (29.2)	202 (27.6)
BMI, mean ± SD, kg/m^2	30.1 ± 8.7	30.0 ± 9.2
Baseline QoL scores, mean ± SD		
Overall RQLQ(S) score	4.0 ± 1.2	4.1 ± 1.2
Individual domain scores		
Activities	4.2 ± 1.3	4.3 ± 1.3
Sleep	3.9 ± 1.5	3.9 ± 1.6
Non-nose/eye symptoms	3.7 ± 1.4	3.7 ± 1.4
Practical problems	4.5 ± 1.3	4.5 ± 1.3
Nasal symptoms	4.7 ± 1.1	4.6 ± 1.1
Eye symptoms	4.2 ± 1.4	4.2 ± 1.4
Emotional	3.5 ± 1.6	3.6 ± 1.5

GSP301, olopatadine 665 µg/mometasone 25 µg; placebo, GSP301 vehicle.
Pooled efficacy data from Studies 1, 2, and 3.
Demographics for the SAS population are shown in TNSS poster.
[a] Includes Asian, American Indian or Alaska native, and native Hawaiian or other Pacific Islander.
BMI, body mass index; FAS, full analysis set; QoL, quality of life; RQLQ(S), Rhinoconjunctivitis Quality of Life Questionnaire –Standardized Activities; SD, standard deviation.

Quality of Life: RQLQ(S)

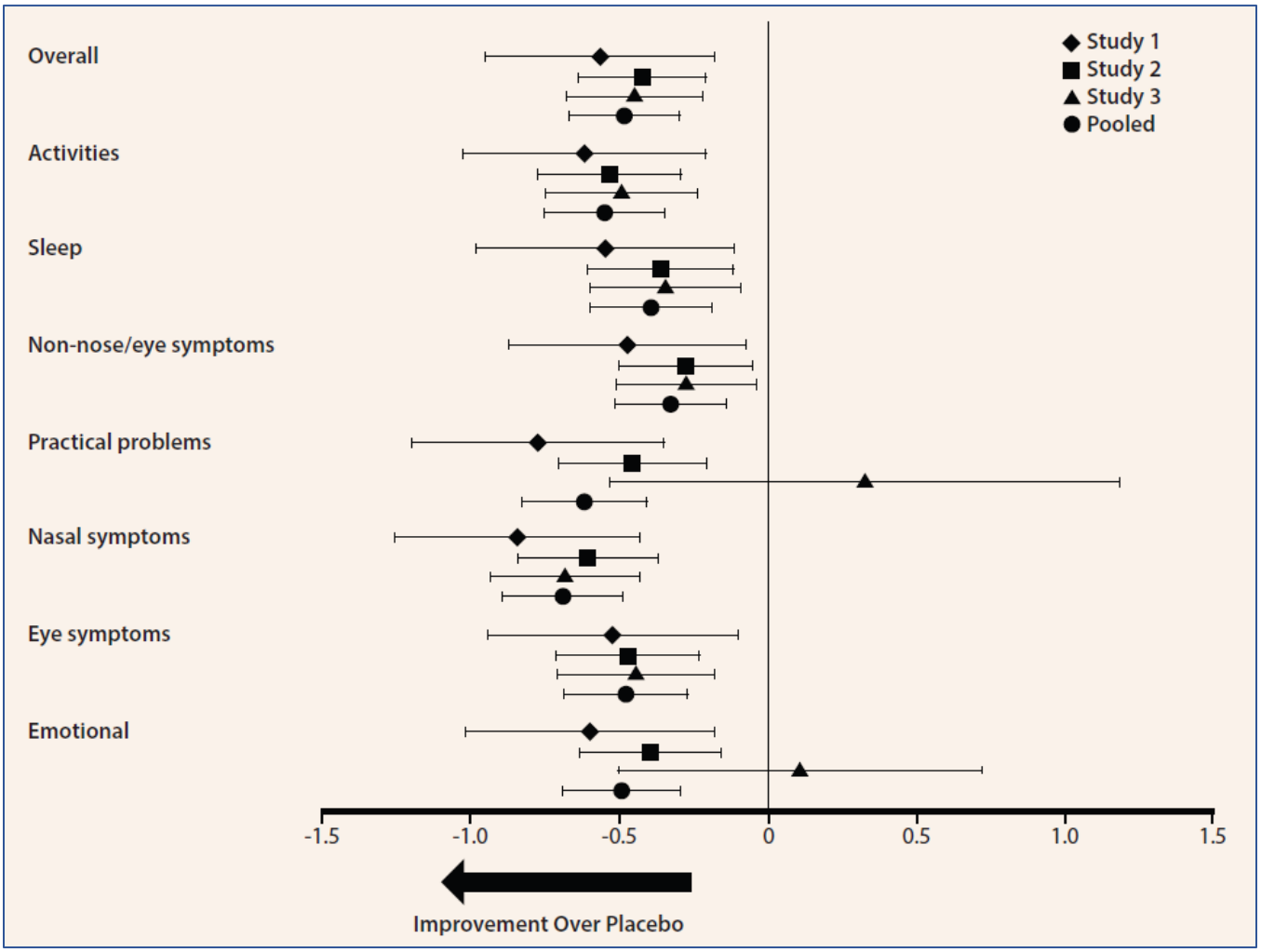
- In the pooled analysis, GSP301 demonstrated significant improvements from baseline to day 15 in overall RQLQ(S) scores compared with placebo (P<0.001; **Table 2**; **Figure 3**); however, the greater improvements (least squares mean difference: -0.48 units) narrowly missed the MCID threshold of 0.50 units
  - For all 7 individual RQLQ(S) domains, GSP301 provided significant improvements vs placebo (P<0.001, all; **Table 2**; **Figure 3**)
- In each individual study, GSP301 significantly improved overall RQLQ(S) scores vs placebo (P≤0.001, all; **Figure 3**)
  - GSP301 also significantly improved all domains vs placebo in the individual Studies 1 and 2 (P<0.05, all); in Study 3, GSP301 significantly improved scores in 5 out of 7 domains vs placebo (**Figure 3**)

Table 2. Mean Difference from Baseline to Day 15 in RQLQ(S) With GSP301 Versus Placebo (FAS) – Pooled Analysis

GSP301 vs Placebo	n1, n2	LSMD	95% CI	*P* value
Overall RQLQ(S) score	725, 707	-0.48	-0.67, -0.30	<0.001*
Individual domain scores				
Activities	735, 717	-0.55	-0.75, -0.35	<0.001*
Sleep	736, 718	-0.40	-0.60, -0.19	<0.001*
Non-nose/eye symptoms	730, 709	-0.33	-0.51, -0.14	<0.001*
Practical problems	735, 718	-0.62	-0.83, -0.41	<0.001*
Nasal symptoms	733, 717	-0.69	-0.89, -0.49	<0.001*
Eye symptoms	736, 718	-0.48	-0.68, -0.27	<0.001*
Emotional	736, 718	-0.49	-0.69, -0.29	<0.001*

GSP301, olopatadine 665 µg/mometasone 25 µg; placebo, GSP301 vehicle. Pooled efficacy data from Studies 1, 2, and 3.
* Indicates statistical significance (*P*<0.05) vs placebo.
CI, confidence interval; FAS, full analysis set; LSMD, least squares mean difference; RQLQ(S), Rhinoconjunctivitis Quality of Life Questionnaire –Standardized Activities.

Figure 3. Mean Change from Baseline to Day 15 in RQLQ(S) With GSP301 Versus Placebo for the Pooled Analysis and Individual Studies (FAS)



GSP301, olopatadine 665 µg/mometasone 25 µg; placebo, GSP301 vehicle.
Efficacy data are presented from each individual study and the pooled studies (Studies 1, 2, and 3).
Data are presented as least squares mean difference with 95% CIs.
CI, confidence interval; FAS, full analysis set; RQLQ(S), Rhinoconjunctivitis Quality of Life Questionnaire –Standardized Activities.

KEY FINDINGS

Safety

- Detailed safety data for the four pooled studies have been reported in the TNSS poster
  - Treatment-emergent AE (TEAE) rates were 13.9% (n/N: 110/789) for GSP301 and 9.5% (74/776) for placebo; most were mild-moderate in severity
  - Only one serious AE (SAE) led to study discontinuation (foot fracture in the placebo group) and no SAEs were considered related to treatment; no deaths occurred

CONCLUSIONS

- In a pooled efficacy analysis of SAR studies conducted with different seasonal allergens, twice-daily GSP301 treatment provided statistically significant improvements in QoL vs placebo
  - For all 7 individual RQLQ(S) domains, GSP301 treatment provided statistically significant improvements vs placebo
- In a pooled safety analysis of 4 SAR studies, GSP301 was well tolerated, with TEAE rates that were generally low and similar across treatments

REFERENCES

1. Patel P, et al. *Ann Allergy Asthma Immunol*. 2018;122(2):160-166.
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.