RAPID ONSET OF ACTION ON NASAL SYMPTOMS AND OCULAR SYMPTOM RELIEF WITH OLOPATADINE/MOMETASONE COMBINATION NASAL SPRAY IN A RAGWEED ENVIRONMENTAL EXPOSURE CHAMBER

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ABSTRACT

Rationale

In a randomized, parallel-group, double-blind, proof-of-concept study, GSP301 fixed-dose combination nasal spray (olopatadine hydrochloride and mometasone furoate) significantly improved instantaneous Total Nasal Symptom Scores (iTNSS, primary endpoint) versus placebo in a ragweed pollen Environmental Exposure Chamber (EEC; previously presented). Onset of action and ocular symptom data are presented here.

Methods

Seasonal allergic rhinitis (SAR) patients (18–65 years; N=180) were equally randomized to GSP301 BID (olopatadine 665 µg/mometasone 25 µg), GSP301 QD (olopatadine 665 µg/mometasone 50 µg), Patanase (olopatadine 665 µg BID), Dymista (azelastine 137 µg/fluticasone 50 µg BID), or placebo (BID) for 14 days. Onset of action was assessed by mean change from baseline in iTNSS from 5 minutes to 4 hours post-dose versus placebo, analyzed via ANCOVA. Instantaneous Total Ocular Symptom Scores (iTOSS) and adverse events were assessed.

Results

Onset of action occurred at 10 minutes post-dose for GSP301 BID (least squares mean difference [95% CI]: -1.26 [-2.30, -0.21], *P*=0.019) and was maintained at later timepoints. Onset of action could not be defined for GSP301 QD, Dymista, or Patanase as statistically significant differences in iTNSS change from baseline between these treatments and placebo were not observed at any 2 consecutive timepoints. Additionally, GSP301 significantly improved iTOSS vs placebo for BID (mean change from baseline to day 14: -1.64 [-2.60, -0.68], *P*=0.001) and QD dosing (-1.20 [-2.15, -0.24], *P*=0.015). All treatments were well tolerated.

Conclusion

In an EEC model, GSP301 BID had a rapid onset of action of 10 minutes and provided significant improvements in ocular symptoms vs placebo. GSP301 QD and BID treatments were well tolerated.

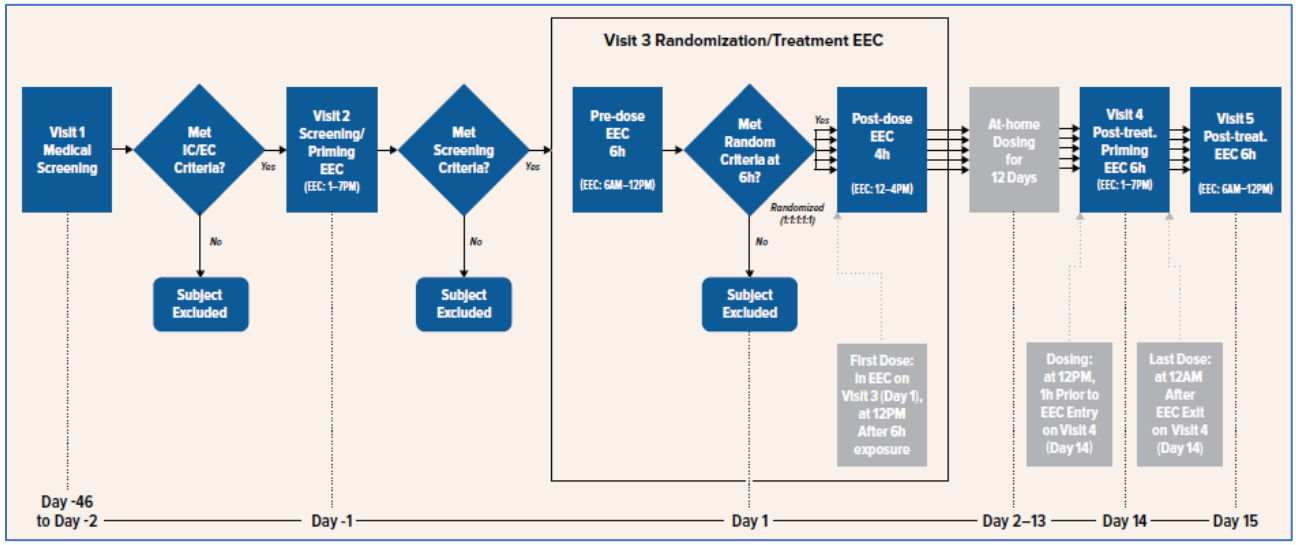
PRESENTED AT THE AMERICAN ACADEMY OF ALLERGY, ASTHMA, AND IMMUNOLOGY &
WORLD ALLERGY ORGANIZATION JOINT CONGRESS
MARCH 2-5, 2018 I ORLANDO, FL

KEY FINDINGS

STUDY DESIGN

- Randomized, double-blind, double-dummy, placebo-controlled, parallel-group proof-of-concept study
- Patients (18 – 65 years of age with a clinical history of SAR for ≥2 years) 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)
- SAR symptoms were assessed at pre-specified timepoints during 4 clinic visits (2, 3, 4, and 5) in an EEC; symptoms were recorded in an electronic diary using the iTNSS

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; Visit 3 EEC was 10 hours, with 6 hours spent in the EEC immediately before the first dose 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 occurred approximately 6 hours after the last dose taken at 12 AM on Day 14. The duration of EEC Visits 2, 4, and 5 was approximately 6 hours each.
EC, exclusion criteria; EEC, environmental exposure chamber; IC, inclusion criteria.

Endpoints

- Onset of action was determined by the mean change from baseline in iTNSS at every time point after the first dose of study treatment (in the 4 hours post-dose at visit 3) versus placebo; starting at pre-dose and from 5 minutes to 4 hours post-dose, a total of 15 timepoints were assessed (**Figure 2**)
- The effect of GSP301 on ocular symptoms was assessed by comparing the mean change from baseline (visit 3) to post-treatment (visit 5) in iTOSS versus placebo
- AEs were monitored
- The primary efficacy endpoint – mean change from baseline (visit 3) to end of treatment (visit 4) in post-dose iTNSS with GSP301 BID and QD versus placebo – has been previously reported[1]; secondary endpoint data for GSP301 BID, QD, and placebo are presented here

RESULTS

Patients

- 180 patients were randomized; at baseline, patients had moderate to severe AR symptoms, with mean iTNSS ranging from 7.6 to 8.2 and mean iTOSS ranging from 4.3 to 4.5 (**Table 1**)
- One patient in the GSP301 QD group discontinued the study due to a family emergency and 1 patient in the placebo group discontinued due to procedural non-compliance

Table 1. Baseline Characteristics

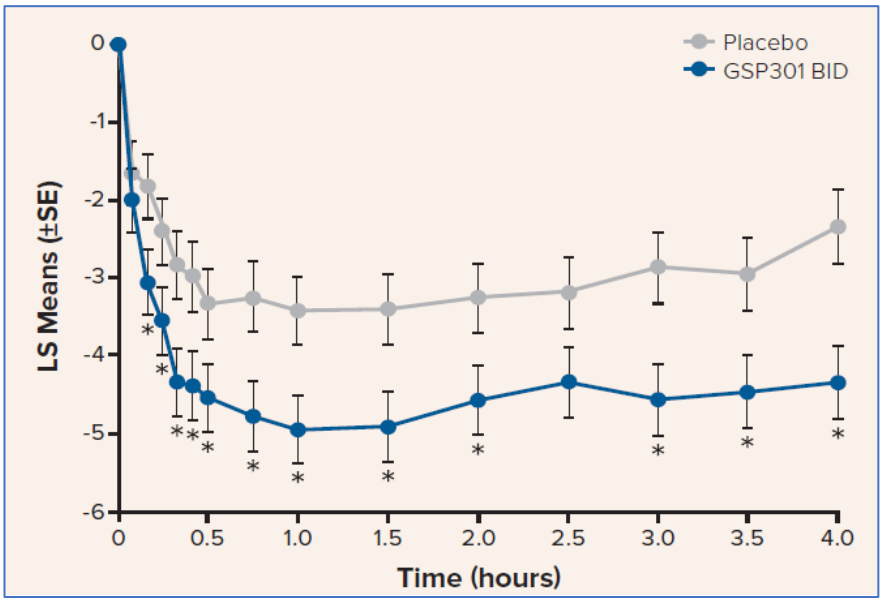
	GSP301 BID (n=36)	GSP301 QD (n=36)	Placebo (n=36)
Demographics			
Age, mean ± SD, y	38.3 ± 10.8	44.9 ± 11.8	42.1 ± 12.5
Sex, n (%)			
Male	22 (61.1)	18 (50.0)	16 (44.4)
Female	14 (38.9)	18 (50.0)	20 (55.6)
Weight, mean ± SD, kg	82.0 ± 19.6	81.7 ± 14.2	76.0 ± 16.5
Race, n (%)			
White	20 (55.6)	14 (38.9)	18 (50.0)
Black	9 (25.0)	13 (36.1)	11 (30.6)
Asian	5 (13.9)	8 (22.2)	7 (19.4)
Other[a]	2 (5.6)	1 (2.8)	0 (0)
Ethnicity, n (%)			
Non-Hispanic or Latino	32 (88.9)	31 (86.1)	35 (97.2)
Hispanic or Latino	4 (11.1)	5 (13.9)	1 (2.8)
Baseline Clinical Characteristics			
iTNSS, mean ± SD[b]	8.1 ± 2.3	8.2 ± 2.1	7.6 ± 2.2
iTOSS, mean ± SD[b]	4.3 ± 1.9	4.5 ± 2.3	4.3 ± 1.8

GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 50 µg.
[a] Includes patients of mixed race and those that did not identify with the other mentioned race categories.
[b] ITT population: GSP301 BID n=36; GSP301 QD n=36; placebo n=35.
BID, twice-daily dosing; iTNSS, instantaneous Total Nasal Symptom Score; iTOSS, instantaneous Total Ocular Symptom Score; QD, once-daily dosing; SD, standard deviation.

Efficacy

- Rapid onset of action for GSP301 BID vs placebo was observed at 10 minutes after the first dose (LSMD [95% CI]: -1.26 [-2.30, -0.21], *P*=0.019) and was maintained at later timepoints except at 2.5 hours (*P*=0.06; **Figure 2**)
  - Statistical significance was not reached for change from baseline in iTNSS vs placebo at any two consecutive timepoints for GSP301 QD, Dymista, or Patanase and thus, onset of action could not be defined for these treatments (data not shown)

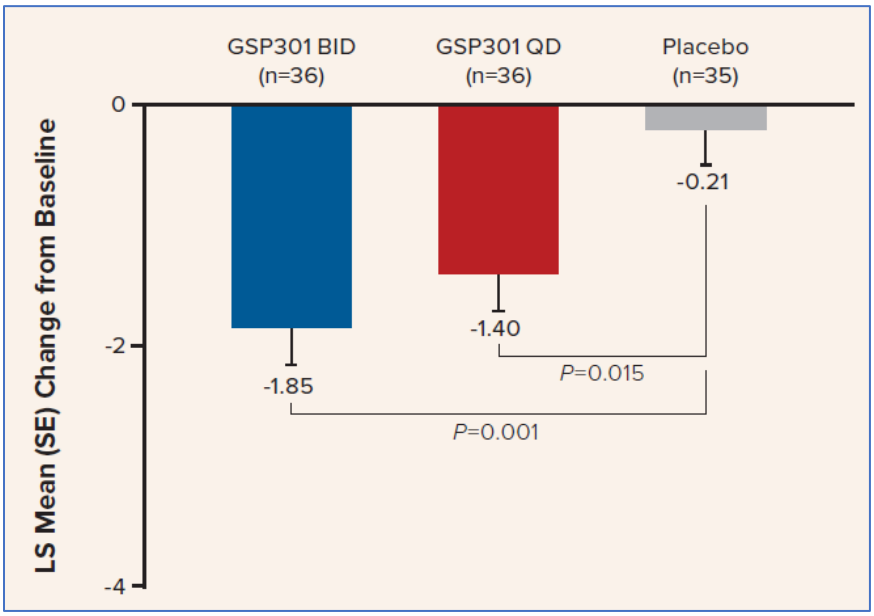
Figure 2. LS Mean (SE) of Average iTNSS Onset of Action for GSP301 BID vs Placebo



GSP301 BID, olopatadine 665 µg/mometasone 25 µg.
*P<0.05 vs placebo.
BID, twice-daily dosing; iTNSS, instantaneous Total Nasal Symptom Score; LS, least squares; SE, standard error.

- GSP301 BID demonstrated significant (statistically significant, P<0.05) improvements on iTOSS from baseline to post-treatment vs placebo (LSMD [95% CI]: -1.64 [-2.60, -0.68], P=0.001; **Figure 3**)
- Similarly, GSP301 QD demonstrated significant improvements in iTOSS compared with placebo (-1.20 [-2.15, -0.24], P=0.015; **Figure 3**)

Figure 3. iTOSS 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.
BID, twice-daily dosing; iTOSS, instantaneous Total Ocular Symptom Score; LS, least squares;
QD, once-daily; SE, standard error.

KEY FINDINGS

Safety

- All TEAEs were mild to moderate and none led to study discontinuation; no serious adverse events (SAEs) or deaths were reported (**Table 2**)

Table 2. Adverse Events

n (%)	GSP301 BID (n=36)	GSP301 QD (n=36)	Placebo (n=36)
Subjects reporting ≥1 TEAE	8 (22.2)	11 (30.6)	6 (16.7)
TEAEs[a]			
Headache	4 (11.1)	6 (16.7)	3 (8.3)
Dysgeusia	2 (5.6)	1 (2.8)	0 (0)
Treatment-related TEAEs	7 (19.4)	5 (13.9)	3 (8.3)
TEAEs leading to withdrawal	0 (0)	0 (0)	0 (0)
SAEs	0 (0)	0 (0)	0 (0)
Deaths	0 (0)	0 (0)	0 (0)

GSP301 BID, olopatadine 665 µg/mometasone 25 µg; GSP301 QD, olopatadine 665 µg/mometasone 50 µg.
[a]Occurring in ≥2% of patients in any treatment group.
BID, twice-daily; QD, once-daily; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- In an EEC model, GSP301 BID treatment demonstrated a rapid onset of action of 10 minutes, which was maintained at all later timepoints except one
- GSP301 BID and QD also demonstrated significant improvements in SAR ocular symptoms versus placebo
- GSP301 BID and QD treatments were well tolerated, with only mild to moderate AEs reported
- These results demonstrate that GSP301 BID is well tolerated and provides rapid and sustained relief of SAR symptoms in adult patients

REFERENCE

1. Patel P, et al. 2017. Poster presented at: 75th annual meeting of the American College of Allergy, Asthma, Immunology.