# EFFICACY AND SAFETY OF OLOPATADINE/MOMETASONE COMBINATION NASAL SPRAY FOR THE TREATMENT OF SEASONAL ALLERGIC RHINITIS

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## ABSTRACT

### Objective

GSP301 nasal spray (NS) is a fixed-dose combination of the antihistamine olopatadine hydrochloride and the corticosteroid mometasone furoate. Efficacy and safety of GSP301 were evaluated in this Seasonal Allergic Rhinitis (SAR) study.

### Methods

In this randomized, double-blind, parallel-group study, eligible patients (≥12 years) with SAR were randomized 1:1:1:1 to GSP301 (olopatadine 665µg/mometasone 25µg BID), olopatadine (665µg BID), mometasone (25µg BID), or placebo for 14 days. The primary endpoint—mean change from baseline in AM and PM reflective Total Nasal Symptom Score (rTNSS)—was analyzed via mixed-effect model repeated measures (MMRM). Adverse events (AEs) were also assessed.

### Results

A total of 1,176 patients were randomized. GSP301 BID treatment statistically significantly improved rTNSS scores vs placebo (least square means difference [95% CI]: -1.09 [-1.49, -0.69]; $P<0.001$) and also showed significant improvement vs olopatadine ($P=0.028$) and mometasone ($P=0.019$). Olopatadine and mometasone significantly improved rTNSS scores vs placebo (olopatadine: $P=0.001$; mometasone: $P=0.002$). Treatment-emergent AEs were reported by 15.6%, 12.6%, 9.6% and 9.5% of patients in the GSP301, olopatadine, mometasone, and placebo groups, respectively.

### Conclusions

GSP301 BID treatment provided statistically significant and clinically meaningful improvements in SAR symptoms versus placebo and versus individual monotherapies. GSP301 BID treatment was well tolerated.

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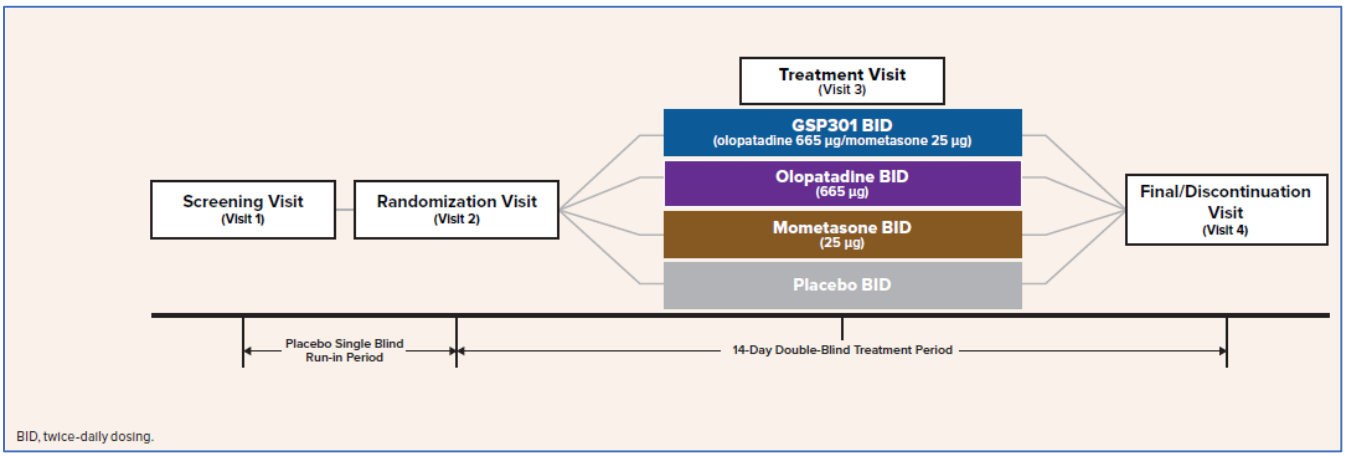
# KEY FINDINGS

## STUDY DESIGN

- Phase 3, randomized, double-blind, parallel-group study (NCT02631551) in patients with SAR during the Fall and mountain cedar pollen seasons (**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 (sneezing, runny nose, itchy nose, and nasal congestion) and non-nasal symptoms (itching/burning, tearing/watering, and redness of eyes, and itching of ears or palate) in a symptom diary
- A difference of 0.23 units in TNSS was considered clinically meaningful (defined as the minimal clinically important difference)[1]
- Safety was monitored via laboratory and physical examinations, ear, nose and throat examinations, vital signs, ECG, and adverse events (AEs)

### Figure 1. Study Design




### Endpoints

- Primary: mean change from baseline to end of treatment in patient-reported AM and PM 12-hour rTNSS over the 14-day treatment period for:
  - GSP301 vs placebo
  - GSP301 vs olopatadine and mometasone monotherapies
  - Olopatadine and mometasone monotherapies vs placebo
- Additional: mean change from baseline to end of 14-day treatment in patient-reported AM and PM 12-hour iTNSS; mean AM and PM reflective individual nasal symptoms over the 14-day treatment period; and safety assessments and AEs

## 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=1,172)
- Safety assessments based on the safety analysis set (SAS) consisting of all patients who received ≥1 dose of study drug (n=1,175)
- Demographic and baseline characteristics were comparable among treatment groups (**Table 1**)

# KEY FINDINGS

## Table 1. Baseline Characteristics

| | GSP301 (n=293) | Olopatadine (n=293) | Mometasone (n=293) | Placebo (n=293) |
|---|---|---|---|---|
| Age, mean ± SD, y | 39.9 ± 14.9 | 39.9 ± 14.6 | 39.2 ± 14.9 | 39.6 ± 14.9 |
| Sex, n (%) | | | | |
| Male | 91 (31.1) | 104 (35.5) | 123 (42.0) | 117 (39.9) |
| Female | 202 (68.9) | 189 (64.5) | 170 (58.0) | 176 (60.1) |
| Race, n (%) | | | | |
| White | 251 (85.7) | 244 (83.3) | 232 (79.2) | 229 (78.2) |
| Black | 30 (10.2) | 41 (14.0) | 50 (17.1) | 60 (20.5) |
| Asian | 7 (2.4) | 4 (1.4) | 8 (2.7) | 3 (1.0) |
| Other[a] | 5 (1.7) | 4 (1.4) | 3 (1.0) | 1 (0.3) |
| Ethnicity, n (%) | | | | |
| Non-Hispanic or Latino | 224 (76.5) | 197 (67.2) | 208 (71.0) | 214 (73.0) |
| Hispanic or Latino | 69 (23.5) | 96 (32.8) | 85 (29.0) | 79 (27.0) |
| rTNSS, mean ± SD[b] | 10.1 ± 1.22 | 10.2 ± 1.25 | 10.2 ± 1.31 | 10.3 ± 1.22 |
| iTNSS, mean ± SD[b] | 9.2 ± 1.80 | 9.4 ± 1.70 | 9.4 ± 1.82 | 9.6 ± 1.77 |

GSP301, olopatadine 665 µg/mometasone 25 µg BID; olopatadine, 665 µg BID; mometasone, 25 µg BID.
[a]Includes American Indian or Alaska native, native Hawaiian or other Pacific Islander.
[b]Full analysis set.
BID, twice-daily dosing; iTNSS, instantaneous Total Nasal Symptom Score; rTNSS, reflective Total Nasal Symptom Score; SD, standard deviation.

## Efficacy

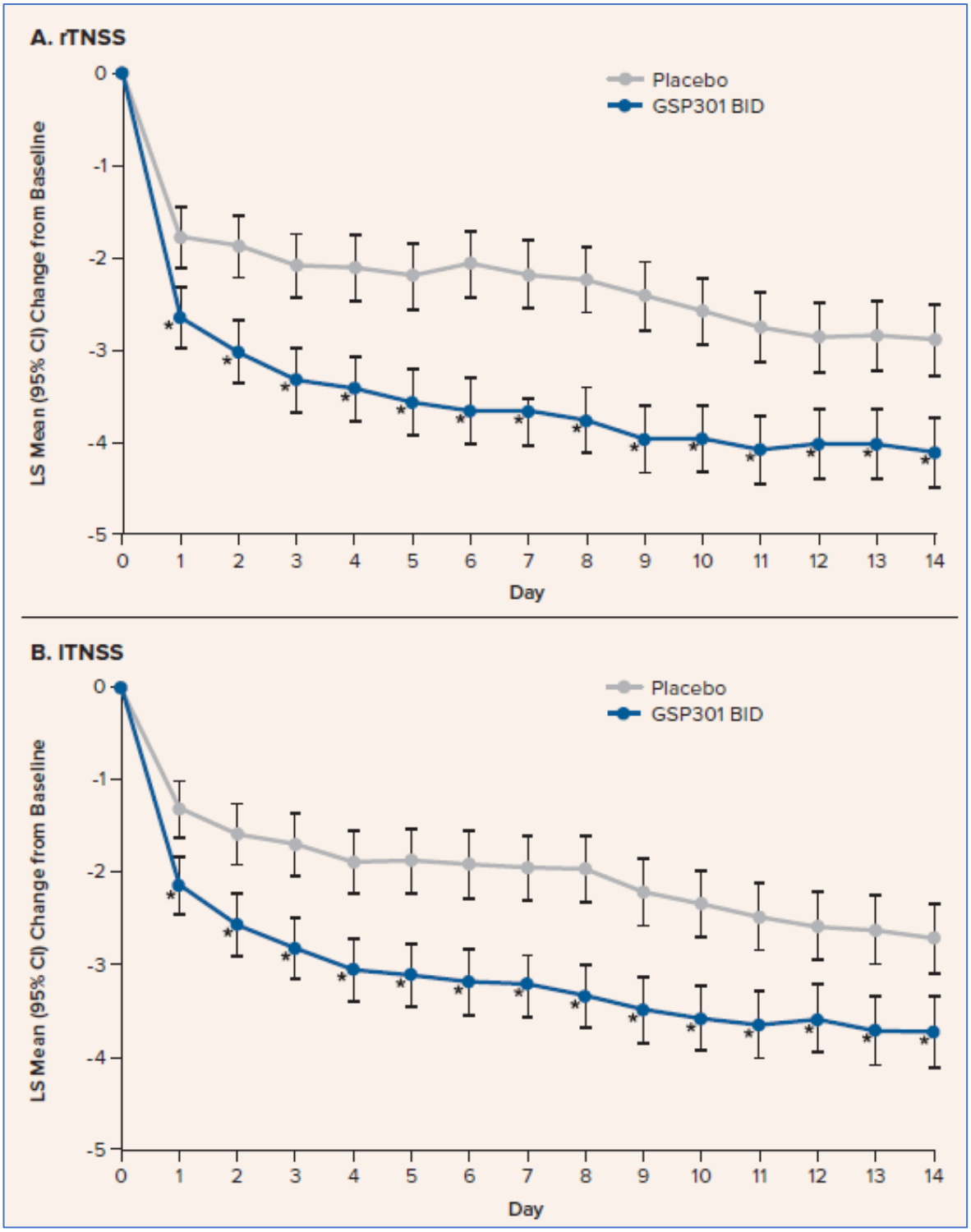
## Table 2. LS Mean Difference in Average AM and PM rTNSS and iTNSS Over 14 Days of Treatment

| Treatment Groups (1 vs 2) | n1, n2 | LSMD | 95% CI | *P* value |
|---|---|---|---|---|
| **rTNSS** | | | | |
| GSP301 vs Placebo | 291, 290 | -1.09 | -1.49, -0.69 | <0.001* |
| GSP301 vs Olopatadine | 291, 290 | -0.44 | -0.84, -0.05 | 0.028* |
| GSP301 vs Mometasone | 291, 293 | -0.47 | -0.86, -0.08 | 0.019* |
| Olopatadine vs Placebo | 290, 290 | -0.64 | -1.04, -0.25 | 0.001* |
| Mometasone vs Placebo | 293, 290 | -0.62 | -1.01, -0.22 | 0.002* |
| **iTNSS** | | | | |
| GSP301 vs Placebo | 291, 290 | -0.94 | -1.32, -0.56 | <0.001* |
| GSP301 vs Olopatadine | 291, 290 | -0.41 | -0.78, -0.03 | 0.035* |
| GSP301 vs Mometasone | 291, 293 | -0.51 | -0.88, -0.13 | 0.008* |
| Olopatadine vs Placebo | 290, 290 | -0.54 | -0.92, -0.16 | 0.005* |
| Mometasone vs Placebo | 293, 290 | -0.44 | -0.81, -0.06 | 0.023* |

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

- GSP301 significantly improved rTNSS and iTNSS vs placebo from baseline to the end of 14-day treatment versus placebo (*P*<0.001; **Table 2**) and from day 1 and on each subsequent day up to day 14 (**Figure 2**), suggesting sustained symptom improvement
- GSP301 also significantly improved all individual nasal symptoms versus placebo over the 14-day treatment period (*P*<0.001, all; **Table 3**)

**Figure 2. LS Mean (95% CI) Change from Baseline in Average AM and PM rTNSS (A) and iTNSS (B) With GSP301 vs Placebo Over 14 Days of Treatment**




GSP301, olopatadine 665 µg/mometasone 25 µg BID.
*$P$<0.05 vs placebo.
BID, twice-daily dosing; CI, confidence interval; LS, least squares; iTNSS, instantaneous Total Nasal Symptom Score; rTNSS, reflective Total Nasal Symptom Score.

### Table 3. LS Mean Difference in Individual Reflective and Instantaneous Nasal Symptom Scores With GSP301 vs Placebo

| Reflective | LSMD (95% CI) | *P* value |
|---|---|---|
| Rhinorrhea | -0.30 (-0.41, -0.19) | <0.001* |
| Nasal congestion | -0.20 (-0.30, -0.09) | <0.001* |
| Nasal itching | -0.23 (-0.34, -0.12) | <0.001* |
| Sneezing | -0.41 (-0.53, -0.29) | <0.001* |
| **Instantaneous** | **LSMD (95% CI)** | ***P* value** |
| Rhinorrhea | -0.29 (-0.39, -0.18) | <0.001* |
| Nasal congestion | -0.19 (-0.29, -0.09) | <0.001* |
| Nasal itching | -0.21 (-0.32, -0.10) | <0.001* |
| Sneezing | -0.29 (-0.41, -0.18) | <0.001* |

GSP301, olopatadine 665 µg/mometasone 25 µg BID.
*indicates significant P values vs placebo.
BID, twice-daily dosing; CI, confidence interval; LSMD, least squares mean difference.

## Safety

- The majority of TEAEs were mild or moderate in severity and were not considered related to treatment (**Table 4**)
  - Only 1 TEAE (dysgeusia) occurred in ≥2% of patients in any treatment group
  - Three patients withdrew due to a TEAE, all in the olopatadine group: bronchitis (n=1), upper respiratory tract infection (n=1), and seizure (n=1)
  - Four patients experienced 8 SAEs (foot fracture, syncope and osteomyelitis [n=1]; diverticulitis, large intestinal obstruction, and large intestinal perforation [n=1]; ischemic stroke [n=1]; peritonsillar abscess [n=1]); none were considered related to study treatment

### Table 4. Adverse Events

| n, (%) | GSP301 (n=293) | Olopatadine (n=293) | Mometasone (n=293) | Placebo (n=293) |
|---|---|---|---|---|
| Patients reporting ≥1 TEAE | 46 (15.7) | 37 (12.6) | 28 (9.6) | 28 (9.6) |
| TEAEs (≥2%) | | | | |
| Dysgeusia | 11 (3.8) | 2 (0.7) | 0 (0) | 0 (0) |
| Patients with a TEAE leading to withdrawal | 0 (0) | 3 (1.0) | 0 (0) | 0 (0) |
| Patients with an SAE | 0 (0) | 2 (0.7) | 1 (0.3) | 1 (0.3) |
| Deaths | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

GSP301, olopatadine 665 µg/mometasone 25 µg BID; olopatadine, 665 µg BID; mometasone, 25 µg BID.
BID, twice-daily dosing; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

## CONCLUSIONS

- In this study, twice-daily (BID) treatment with GSP301 fixed-dose combination nasal spray resulted in significant, sustained, and clinically meaningful[1] improvements in SAR nasal symptoms compared with placebo and component monotherapies
- GSP301 was well tolerated with similar incidences of AEs compared with placebo or individual monotherapies
- These results demonstrate that GSP301 BID is efficacious and well tolerated for the treatment of nasal symptoms associated with SAR in adult and adolescent patients 12 years of age and older

## REFERENCE

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