# A Multi-Center, Open-Label Extension Study to Assess the Long-term Safety/Tolerability and Pharmacokinetics, and Explore the Efficacy of Sofpironium Bromide Gel, 15% Applied Topically to Children and Adolescents, 9 to 16 Years of Age, with Primary Axillary Hyperhidrosis

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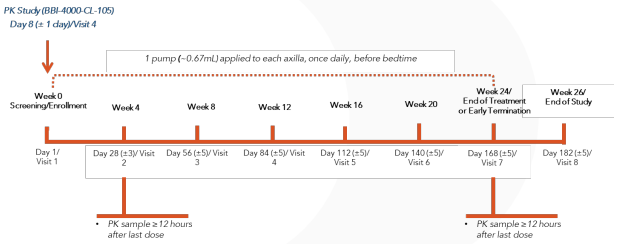
## Introduction

~2.1% of the US population aged <18 years has primary hyperhidrosis (HH); ~65% have axillary HH. Long-term safety/tolerability and efficacy of topical HH treatments have rarely been studied in pediatric patients. Sofpironium bromide is a retro-metabolically designed analog of glycopyrrolate (anticholinergic) in development for topical treatment of primary axillary HH. Absorbed drug is rapidly metabolized, potentially allowing optimal local therapeutic effect with minimal systemic effects.

## Procedures

21 of 25 subjects (age 9-16 yrs) with primary axillary HH of ≥6 months duration, completing a previous 1-week safety and pharmacokinetic (PK) study (BBI-4000-CL-105), were enrolled. Objectives were to assess safety/tolerability and PK, and explore efficacy of sofpironium bromide gel, 15% applied to both axillae for 24 weeks.




### Table 1. Summary of TEAEs

| | SB GEL, 15% (N=21) |
|---|---|
| Subjects with TEAEs | 7 (33.3%) |
| Number of TEAEs | 21 |
| Subjects with Treatment-Related AEs | 4 (19.0%) |
| Subjects with SAEs | 0 |
| Subject Discontinuations Due to TEAE | 2 (9.5%) |
| TEAE by Severity (all TEAEs) | |
| Mild | 5 (23.8%) [8] |
| Moderate | 5 (23.8%) [13] |
| Severe | 0 |
| TEAE by Severity (relationship – possibly, probably or definitely related) | |
| Mild | 3 (14.3%) [4] |
| Moderate | 4 (19.0%) [11] |
| Severe | 0 |

Note: A TEAE is defined as any AE occurring on or after first dose. The first number corresponds to the count of unique subjects and percentage, while the second number in [n] is the count of raw events. Subjects are counted only once at the strongest relationship to the study medication.

### Table 2: Frequency of TEAEs

| PREFERRED TERM | SB GEL, 15% (N=21) |
|---|---|
| Application site pain | 2 (9.5%) [3] |
| Application site pruritis | 2 (9.5%) [2] |
| Acne | 1 (4.8%) [1] |
| Anxiety | 1 (4.8%) [1] |
| Burning sensation | 1 (4.8%) [1] |
| Chapped lips | 1 (4.8%) [1] |
| Decreased appetite | 1 (4.8%) [1] |
| Dermatitis Atopic | 1 (4.8%) [1] |
| Dry eye | 1 (4.8%) [1] |
| Dry mouth | 1 (4.8%) [1] |
| Dysmenorrhea | 1 (4.8%) [1] |
| Erythema | 1 (4.8%) [1] |
| Hydriasis | 1 (4.8%) [1] |
| Nausea | 1 (4.8%) [1] |
| Pruritis | 1 (4.8%) [1] |
| Rash | 1 (4.8%) [1] |
| Skin infection | 1 (4.8%) [1] |
| Vision blurred | 1 (4.8%) [1] |
| Hydriasis | 1 (4.8%) [1] |
| Nausea | 1 (4.8%) [1] |

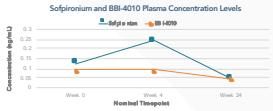
Note: A TEAE is defined as any AE occurring on or after first dose. The first number corresponds to the count of unique subjects and percentage, while the second number in [n] is the count of raw events.

### Table 3: Summary of Local Tolerability

| ASSESSMENT | SB GEL, 15% (N=21) | | | | |
|---|---|---|---|---|---|
| | Any Present | Minimal | Mild | Moderate | Severe |
| Subjects with any Local Symptoms by Worst Severity | 10 (47.6%) | 4 (19.0%) | 1 (4.8%) | 5 (23.8%) | 0 |
| Burning | 4 (19.0%) | 1 (4.8%) | 1 (4.8%) | 2 (9.5%) | 0 |
| Stinging | 3 (14.3%) | 1 (4.8%) | 1 (4.8%) | 1 (4.8%) | 0 |
| Itching | 7 (33.3%) | 2 (9.5%) | 2 (9.5%) | 3 (14.3%) | 0 |
| Scaling | 1 (4.8%) | 1 (4.8%) | 0 | 0 | 0 |
| Erythema | 9 (42.9%) | 4 (19.0%) | 2 (9.5%) | 3 (14.3%) | 0 |

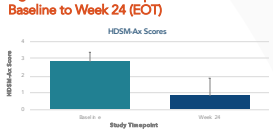
Note: The severity shown is the greatest severity reported for a particular assessment (burning/stinging/itching/scaling/erythema). Maximum severity assessed for either axilla is reported.

### Figure 1: Sofpironium and BBI-4010 Plasma Concentrations (Week 0 to Week 24)



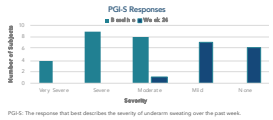

The pharmacokinetic population includes all enrolled subjects who applied at least one dose of study drug and had at least one PK sample for analysis while on Study BBI-4000-CL-108. The LLOQ of this assay in plasma is 0.0555 ng/mL for both sofpironium and BBI-4010. Concentrations that are reported as BLQ have been set to 0 for the descriptive statistics for the drug concentration summary.

### Figure 2: HDSM-Ax Responses from Baseline to Week 24 (EOT)



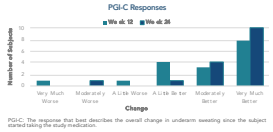

*The Hyperhidrosis Disease Severity Measure-Axillary® (HDSM-Ax) is a validated 11-item measure of axillary hyperhidrosis severity and frequency with a 5-point scale for each item. A change of -1.00 from the mean baseline score has been defined to represent clinically meaningful improvement.

### Figure 3: PGI-S Responses from Baseline to Week 24 (EOT)




PGI-S: The response that best describes the severity of underarm sweating over the past week.

### Figure 4: PGI-C Responses at Week 12 and Week 24 (EOT)




PGI-C: The response that best describes the overall change in underarm sweating since the subject started taking the study medication.

## Results

Mean age (SD) 13.3 (2.29) years. 16 subjects completed this 24-week study. 7 had treatment emergent adverse events (TEAEs); 4 with AEs related to study drug, including expected systemic anticholinergic AEs (blurred vision, dry mouth, dry eyes, mydriasis) and local events (pain, pruritus, rash, erythema). 2 subjects discontinued due to TEAEs, including dry eye, dry mouth, local pruritus, local rash. The majority (52.4%) of subjects did not have any local symptoms/signs, and none observed were severe in nature. PK did not show evidence of drug/major metabolite accumulation, with most subjects having concentrations not quantifiable. The validated patient-reported outcome, Hyperhidrosis Disease Severity Measure-Axillary (HDSM-Ax), showed mean (SD) change from baseline (from previous study) to Week 24 of this study of -1.91 (1.038). A -1.00 change shows clinically meaningful improvement.

## Conclusion

In this 24-week study in pediatric subjects sofpironium bromide, 15% was safe/well tolerated. Majority of subjects had no TEAE, and there were no severe or serious AEs. There was no evidence of drug accumulation. There was indication of clinically meaningful improvement in axillary HH.

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