# A Multi-Center, Open-Label Study to Assess Pharmacokinetics (PK), Safety and Tolerability of Sofpironium Bromide Gel, 15% Applied Topically to Children and Adolescents, ≥9 to <17 Years of Age, with Axillary Hyperhidrosis

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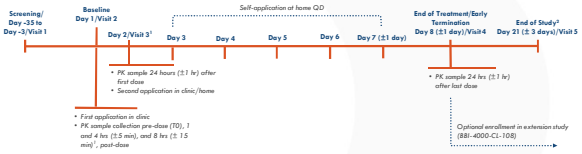
## Introduction

Excessive sweating affects approximately 15 million Americans. Sofpironium bromide is a retro-metabolically designed analog of glycopyrrolate (anticholinergic) in development for the topical treatment of axillary hyperhidrosis. Retro-metabolically designed drugs are rapidly metabolized in the bloodstream, allowing for potentially optimal therapeutic effect at application sites with minimal systemic side effects .

Primary hyperhidrosis has a prevalence rate of 2.1% for individuals <18 years of age with any area of involvement, with approximately 65% (1.4%) experiencing axillary hyperhidrosis.[1] The safety, tolerability and efficacy of topical treatments for axillary hyperhidrosis have rarely been studied in the pediatric population.

## Methods

Twenty-five subjects ranging in age from 9 to 16 years with axillary hyperhidrosis of at least 6 months duration were enrolled. The objectives of the study were to assess systemic exposure, safety and effectiveness of sofpironium bromide gel, 15% following application to both axillae for 7 (± 1) days. Based on a previously observed half-life of 5 to 6 hours in adult subjects, steady-state was anticipated within 24 hours; thus, a 1-week treatment duration was deemed sufficient to evaluate systemic absorption after repeat administration.




[1] May be done as a home visit
[2] Only complete if subject does not continue in the optional extension study (BBI-4000-CL-108)

**Table 1. Demographics and Baseline Characteristics**

| VARIABLE | SB GEL, 15% (N=25) |
|---|---|
| **Age (years)** | |
| Mean (SD) | 13.4 (2.14) |
| Min, Max | 9, 16 |
| **Gender** | |
| Male | 12 (48.0%) |
| Female | 13 (52.0%) |
| **HDSM-Ax** | |
| Mean (SD) | 2.76 (0.557) |
| Min, Max | 1.7, 3.7 |
| **PGI-S** | |
| None | 0 (0.0%) |
| Mild | 0 (0.0%) |
| Moderate | 9 (36.0%) |
| Severe | 12 (48.0%) |
| Very Severe | 4 (16.0%) |

**Table 2: Summary of TEAEs[1,2]**

| | SB GEL, 15% (N=25) |
|---|---|
| **Subjects with TEAEs** | **3 (12.0%)** |
| **Number of TEAEs** | **4** |
| Dry Eye | 1 (4.0%, mild) |
| Vision Blurred | 1 (4.0%, moderate) |
| Influenza | 1 (4.0%, moderate) |
| Urinary Hesitation | 1 (4.0%, mild) |
| **Subjects with SAEs** | **0 (0.0%)** |
| **Discontinuations Due to TEAEs** | **0 (0.0%)** |

**All data presented are for the study safety population**

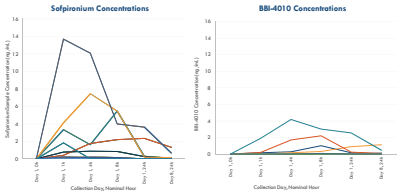
[1]A treatment emergent AE (TEAE) is defined as any AE occurring on or after first dose.
[2]Subjects are counted only once at the strongest relationship to the study medication.

**Table 3: Summary of Local Tolerability at Day 8[3]**

| | Burning | Itching | Stinging | Scaling | Erythema |
|---|---|---|---|---|---|
| **Minimal** | 1 (4.0%) | 3 (12.0%) | 2 (8.0%) | 0 (0.0%) | 3 (12.0%) |
| **Mild** | 1 (4.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (8.0%) |
| **Moderate** | 1 (4.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| **Severe** | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |

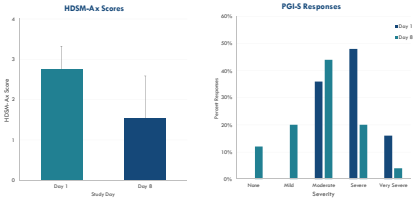
[3]Maximum severity assessed for either axilla is reported.

**Figure 1: Sofpironium and BBI-4010 Plasma Concentrations (Day 1 to Day 7)[4,5,6]**




[4]PK Population includes all 25 subjects.
[5]A total of 14 subjects had no quantifiable sofpironium through the PK time-course.
[6]A total of 19 subjects had no quantifiable BBI-4010 through the PK time-course.
[7]Limit of quantification (LOQ) of 0.050 ng/mL for sofpironium and BBI-4010

**Figure 2: HDSM-Ax and PGI-S Responses from Baseline to Day 8 (EOT)[8,9]**




[8]The Hyperhidrosis Disease Severity Measure-Axillary© (HDSM-Ax) is an 11-item measure of axillary hyperhidrosis severity. A change of -1.00 has been defined to represent clinically meaningful improvement. [9]The Patient Global Impression of Severity (PGI-S) scale is a global index that may be used to rate the severity of a specific condition.

## Results

Following topical application of sofpironium gel, sofpironium and its primary metabolite (BBI-4010) were detected in 11 subjects and 6 subjects, respectively. Systemic exposure to sofpironium and BBI-4010 was typically minimal following the first dose (Day 1) and after multiple doses (Day 8; 24 hours after the last dose). There was no evidence of accumulation.

Four treatment emergent adverse events (TEAEs) were observed, including one of influenza. The remaining three (dry eyes, blurred vision, and urinary hesitation) were expected systemic anticholinergic symptoms. No subject was withdrawn from the study due to an adverse event (AE), and no concomitant medication was necessary.

For the validated patient-reported outcome measures Hyperhidrosis Disease Severity Measure-Axillary (HDSM-Ax; ≥12 years of age) and HDSM-Ax-Child (≥9 to <12 years of age), changes from baseline to Day 8 in mean scores ranged from -3.4 to 0.3 with a mean of -1.23 and a median change of -1.00. A change of -1.00 has been defined to represent clinically meaningful improvement. Similar improvements in the severity of underarm sweating were reported based on the Patient Global Impression of Severity (PGI-S) scale at Day 8.

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## Conclusion

Sofpironium bromide, an investigational agent, has the potential to address an unmet need for a noninvasive, topical primary axillary hyperhidrosis treatment, which is safe and effective for use in the pediatric population. Pharmacokinetic findings were consistent with previous investigational evaluations in adults where systemic sofpironium and BBI-4010 concentrations were also variable, sporadic, and minimal.

As anticipated with retro-metabolic drug design, sofpironium bromide exhibited low numbers of systemic anticholinergic AEs, and all were mild or moderate in severity and transient, with no treatments discontinuations. Clinically meaningful improvements in the frequency and severity of underarm sweating were reported as early as Day 8.

## References

[1]Doolittle J, Walker P, Mills T, Thurston J. Hyperhidrosis; an update on prevalence and severity in the United States. Arch Dermatol Res. 2016; 308:743-749.