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 (BBI-4000-CL-108)

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Background

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

Approximately 2.1% of individuals <18 years of age have primary hyperhidrosis with ~65% having axillary hyperhidrosis.[1] The long-term safety, tolerability and efficacy of topical treatments for axillary hyperhidrosis have rarely been studied in the pediatric population.

Objective

Evaluate the long-term safety, tolerability and pharmacokinetics of topically applied sofpironium bromide gel, 15% for the treatment of axillary hyperhidrosis in pediatric subjects, as well as to explore efficacy.

Methods

Twenty-one subjects with primary axillary hyperhidrosis of ≥6 months duration ranging in age from 9 to 16 years, who had participated in and completed a previous 1-week safety and pharmacokinetic (PK) study (BBI-4000-CL-105), were enrolled and treated with sofpironium bromide gel, 15% applied to the axillae for 24 weeks.

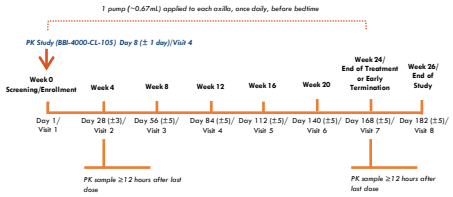


Table 1: Incidence & Severity of TEAEs (n=21)

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]
TEAE by Severity (relationship – possibly, probably or definitely related)	
Mild	3 (14.3%) [4]
Moderate	4 (19.0%) [11]

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 Anticholinergic TEAEs (≥5%) (n=21)

Dry Eye	1 (4.8%) [1]
Dry Mouth	1 (4.8%) [1]
Mydriasis	1 (4.8%) [1]
Vision Blurred	1 (4.8%) [1]

Table 3: Local Site Reactions (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 Concentration Levels

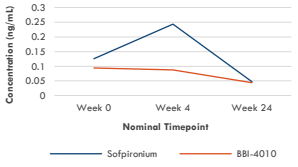
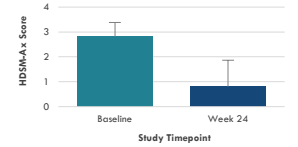
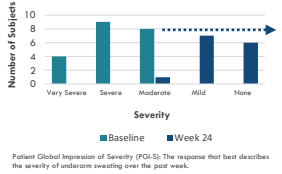


Figure 2: Hyperhidrosis Disease Severity Measure-Axillary (HDSM-Ax) Scores



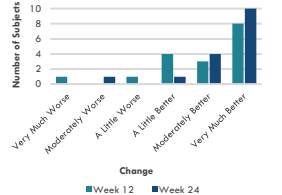
The Hyperhidrosis Disease Severity Measure-Axillary© (HDSM-Ax) is a validated 11-item measure of axillary hyperhidrosis severity and frequency with a 5-point scale for each item. A change of -1.00 from the mean baseline score has been defined to represent clinically meaningful improvement.

Figure 3: Patient Global Assessment of Severity (PGI-S)



Patient Global Impression of Severity (PGI-S): The response that best describes the severity of underarm sweating over the past week.

Figure 4: Change in Global Assessment of Severity (PGI-C)



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

Results

The mean age (SD) of the subjects was 13.3 (2.29) years. Sixteen subjects completed 24-weeks of treatment. Seven subjects had treatment emergent adverse events (TEAEs). Four subjects had TEAEs that were considered related to study drug, which included expected systemic anticholinergic effects (blurred vision, dry mouth, dry eyes, mydriasis) and local site reactions (pain, pruritus, rash, erythema). Two subjects discontinued the study due to adverse events, which included dry eye, dry mouth, pruritus and rash.

The majority of subjects did not have any local signs or symptoms and none were severe. Pharmacokinetic analysis did not show any evidence of sofpironium or BBI-4010 (major metabolite) accumulation, with most subjects having plasma concentrations that were not quantifiable. For the validated patient-reported outcome measure Hyperhidrosis Disease Severity Measure-Axillary (HDSM-Ax), the mean (SD) change from baseline (from study BBI-4000-CL-105) to Week 24 of this study was -1.91 (1.038). A change of -1.00 represents clinically meaningful improvement.

Conclusion

In this 24-week study in the pediatric population, sofpironium bromide gel, 15% appeared safe and generally well tolerated. The majority of subjects did not report any TEAEs, and there were no severe or serious AEs. There was no evidence of drug accumulation. There was clinically meaningful improvement in axillary hyperhidrosis.

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.

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