

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 sofopironium bromide gel, 15% applied to both axillae for 24 weeks.



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.

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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%) [3]
Moderate	5 (23.8%) [1, 3]
Severe	0
TEAE by Severity (relationship = possibly, probably or definitely related)	
Mild	3 (14.3%) [4]
Moderate	4 (19.0%) [1, 1]
Severe	0

Note: A TEAE is defined as any AE occurring on or after first dose. The first number corresponds to the count of events related to the treatment, while the second number (in brackets) is the count of the event. Subjects are counted only once for 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%) [2]
Application site pruritus	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]
Mydriasis	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]
Mydriasis	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 events related to the treatment, while the second number (in brackets) is the count of the event.

Table 3: Summary of Local Tolerability

ASSESSMENT	Any Present	Minimal	Mild	Moderate	Severe
Subjects with any Local Symptoms by Worst Severity	10 (47.6%)	4 (19.0%)	1 (4.8%)	2 (9.5%)	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 predominantly reported for a particular assessment (burning, stinging, itching, scaling, pruritus). Maximum severity assessed for other scales 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-105. The LLOQ of the assay is plasma is 0.0055 ng/mL for both Sofpironium and BBI-4010. Concentrations that are reported as ND have been set as 0.2 for the descriptive statistics for the drug concentration summary.

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



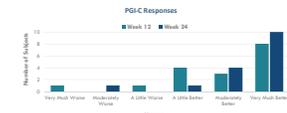
The Hyperhidrosis Disease Severity Measure-Axillary (HDSM-Ax) is a validated 11-item measure of axillary hyperhidrosis severity and frequency with a 5-point scale for each item. A change of 1.00 from the mean baseline score has been defined to represent clinically meaningful improvement.

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



PGI-S: The response that best describes the severity of axillary 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 sweating over the subject's current taking the study medication.

Conclusion

In this 24-week study in pediatric subjects sofopironium 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.