An Open-Label Pilot Study to Evaluate the Effect of Occlusion on the Pharmacokinetics, Safety and Tolerability of Topical Sofpironium Bromide Gel, 15% in Healthy Adult Subjects (BBI-4000-CL-109)

Brandon Kirsch, MD[1], Danielle Armas, MD[2], Deepak Chadha, MS, MBA, RAC[3]

[1]Kirsch Dermatology, Naples, FL, [2]Celerion, Inc., Tempe, AZ, [3]Brickell Biotech, Inc., Boulder, CO

Background

Sofpironium bromide is a retro-metabolically designed analog of glycopyrrolate (anticholinergic) in development for the topical treatment of primary axillary hyperhidrosis. In a prior maximum-use pharmacokinetic study (MUPK, BBI-4000-CL-102), application of sofpironium bromide gel, 15% to the axillae, thighs and palms (3-fold, ~519 mg) had no meaningful impact on systemic exposure, safety or tolerability compared with application to the axillae only (~173 mg).

Objective

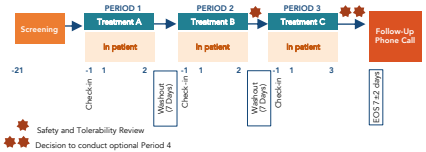
To assess if occlusion of topically applied sofpironium bromide gel, 15%, at an even higher supratherapeutic dose than in the prior MUPK study, substantially increased systemic exposure to sofpironium compared with the intended therapeutic dosing to the axillae only, and inform recommendations for a planned thorough QT (TQT) study.

Methods

This was an open-label, 3-period, pharmacokinetic, safety and tolerability phase 1 study. Twelve healthy adult male and female subjects aged ≥18 to ≤55 years were enrolled.

- On Day 1 of Period 1, all subjects received a single dose of sofpironium bromide gel, 15%, topically *without occlusion* to the axillae (~173 mg, intended therapeutic dose) (Treatment A).
- On Day 1 of Period 2, all subjects received a single dose of sofpironium bromide gel, 15%, topically *without occlusion* to the axillae (1 actuation to each axilla), upper arms (1 actuation to each arm), thighs (2 actuations to each thigh), and abdomen (4 actuations) (6-fold, ~1038 mg, supratherapeutic dose) (Treatment B).
- On Day 1 of Period 3, all subjects received a single dose of sofpironium bromide gel, 15%, topically *with occlusion* to the axillae (1 actuation to each axilla), upper arms (1 actuation to each arm), thighs (2 actuations to each thigh), and abdomen (4 actuations) (6-fold, ~1038 mg, supratherapeutic dose) (Treatment C).

There was a washout period of at least 7 days between dosing periods.



Results

Sofpironium bromide gel, 15% appeared safe and generally well tolerated by subjects in all treatment groups.

- Following the supratherapeutic dose (6-fold) of sofpironium bromide gel, 15% unoccluded, the C_{max} for sofpironium increased by 120%, compared with an unoccluded intended therapeutic dose.
- Following the supratherapeutic dose (6-fold) of sofpironium bromide gel, 15% occluded, the C_{max} for sofpironium increased by 231%, compared with an unoccluded intended therapeutic dose.
- Following the supratherapeutic dose (6-fold) of sofpironium bromide gel, 15% occluded, the C_{max} for sofpironium increased by 50%, compared with an unoccluded supratherapeutic dose.

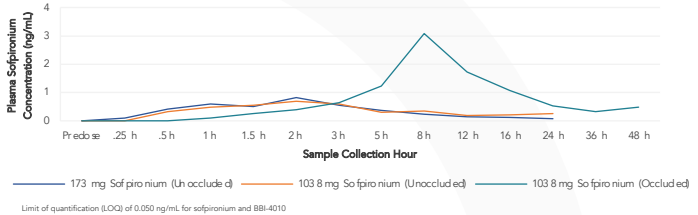
Conclusion

Following a single, supratherapeutic, occluded dose of sofpironium bromide gel, 15%, there was 3-fold higher peak plasma concentration of sofpironium compared with therapeutic unoccluded dosing to the axillae only. As a result, a single, supratherapeutic application of sofpironium bromide gel, 15% under occlusion was thought appropriate for characterization of potential cardiac safety issues as part of a planned TQTc study. Overall, sofpironium bromide gel, 15% appeared safe and well tolerated, and there were no remarkable findings in the safety assessments for clinical laboratory measurements and vital signs.

Funding Statement

Brickell Biotech, Inc. supported the study and preparation of this abstract.

Figure 1: Median Plasma Sofpironium Concentration (Evaluable Pharmacokinetic Population)



Limit of quantification (LOQ) of 0.050 ng/mL for sofpironium and BBI-4010

Table 1: Adverse Event Frequency by Treatment – Number of Subjects Reporting the Event (% of Subjects Dosed) (Safety Population) (≥5%)

	Treatment			
ADVERSE EVENT	**Treatment A**	**Treatment B**	**Treatment C**	**Total**
Number of Subjects Dosed	**12 (100%)**	**12 (100%)**	**12 (100%)**	**12 (100%)**
Number of Subjects With TEAEs	**5 (42%)**	**2 (17%)**	**9 (75%)**	**10 (83%)**
Number of Subjects Without TEAEs	**7 (58%)**	**10 (83%)**	**3 (25%)**	**2 (17%)**
Application site erythema	0 (0%)	0 (0%)	7 (58%)	7 (58%)
Application site irritation	0 (0%)	0 (0%)	1 (8%)	1 (8%)
Application site laceration	0 (0%)	0 (0%)	1 (8%)	1 (8%)
Application site pain	1 (8%)	0 (0%)	4 (33%)	4 (33%)
Application site pruritus	0 (0%)	0 (0%)	5 (42%)	5 (42%)
Application site warmth	0 (0%)	0 (0%)	3 (25%)	3 (25%)
Dermatitis contact	2 (17%)	2 (17%)	0 (0%)	3 (25%)
Dizziness	1 (8%)	0 (0%)	0 (0%)	1 (8%)
Dry mouth	0 (0%)	0 (0%)	1 (8%)	1 (8%)
Eye pain	0 (0%)	0 (0%)	1 (8%)	1 (8%)
Skin laceration	1 (8%)	0 (0%)	0 (0%)	1 (8%)
Vision blurred	0 (0%)	0 (0%)	1 (8%)	1 (8%)

Adverse Event Frequency by Treatment – Number of Subjects Reporting the Event (% of Subjects Dosed) (Safety Population) (≥5%).
A TEAE is defined as any AE occurring on or after first dose.