Glycopyrronium Tosylate for the Treatment of Primary Axillary Hyperhidrosis: Prior Treatment Analyses from the ATMOS-1 and ATMOS-2 Phase 3 Randomized Controlled Trials

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INTRODUCTION

- Hyperhidrosis, which is excessive sweating beyond that physiologically required to maintain normal thermal regulation, affects approximately 4.8% of the US population[1]
- Effective management of hyperhidrosis can significantly improve quality of life[2,3]; however, approved therapeutic options are limited and are often invasive, painful, or time-consuming
- Axillary Hyperhidrosis Patient Measures (AHPM), consisting of the 4-item Axillary Sweating Daily Diary (ASDD), 6 Weekly Impact (WI) items, and a single-item Patient Global Impression of Change (PGIC),[4,5] were developed in consultation with the FDA and in consideration of FDA guidance on patient-reported outcomes
  - ASDD axillary sweating severity item (Item 2) was specifically developed and validated as an endpoint to support regulatory approval[4]
- Glycopyrronium tosylate (GT; formerly DRM04) is a topical cholinergic receptor antagonist that is under evaluation for the treatment of primary axillary hyperhidrosis
- The efficacy and safety of GT in patients ≥9 years of age with primary axillary hyperhidrosis have been evaluated in two phase 3 trials (ATMOS-1 and ATMOS-2),[6] and the primary results have been previously reported[7]

OBJECTIVE

- To evaluate the impact of prior hyperhidrosis treatment on GT efficacy, the results from ATMOS-1 and ATMOS-2 were analyzed based on whether study patients had prior treatment (PT; self-reported) or not (No PT)

METHODS

ATMOS-1 and ATMOS-2 Study Design

- ATMOS-1 (NCT02530281) and ATMOS-2 (NCT02530294) were parallel-group, 4-week, double-blind phase 3 trials in which patients with primary axillary hyperhidrosis were randomized (2:1) to GT (3.75% topical solution) or vehicle[7]
- Eligible patients
  - ≥9 years of age
  - Primary axillary hyperhidrosis for ≥6 months
  - Gravimetrically-measured sweat production of ≥50 mg/5 min in each axilla
  - ASDD Item 2 ≥4 (numeric rating scale 0 to 10)
  - Hyperhidrosis Disease Severity Scale (HDSS) ≥3
- Patients were excluded for history of a condition that could cause secondary hyperhidrosis; new or modified psychotherapeutic medications within 2 weeks; or treatment with medications having systemic anticholinergic activity, centrally acting alpha-2 adrenergic agonists, or beta-blockers within 4 weeks unless on a stable dose for ≥4 months
- Exclusion criteria specified for prior/concomitant treatments included the following
  - Prior surgical procedure or treatment with a medical device for axillary hyperhidrosis
  - Treatment with iontophoresis for axillary hyperhidrosis within 4 weeks
  - Treatment with botulinum toxin for axillary hyperhidrosis within 1 year
  - Axillary use of nonprescription antiperspirants within 1 week or prescription antiperspirants within 2 weeks

Assessments

- Efficacy assessments included gravimetric sweat production, ASDD Item 2, HDSS, and Dermatology Life Quality Index (DLQI)
  - Patients <16 years of age completed a modified, 2-item version of the ASDD (ASDD-C) and patients ≤16 completed the Children's DLQI (CDLQI)
- Coprimary endpoints were ASDD Item 2 response rate (≥4-point improvement from Baseline) and mean absolute change in sweat production (average of both axillae) at Week 4
- Safety assessments included treatment-emergent adverse events (TEAEs)

Analysis of Prior-Treatment Subgroups

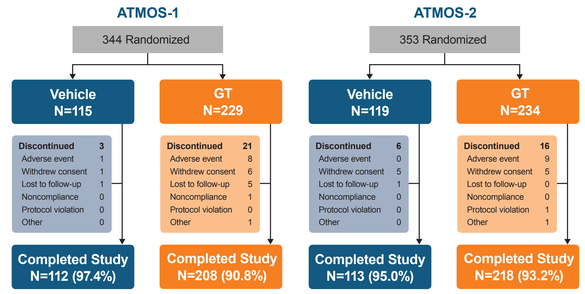
- In this descriptive post hoc analysis, data for the intent-to-treat (ITT) population (all randomized patients dispensed study drug) were stratified by whether study patients had PT or No PT for the following endpoints at Week 4:
  - ASDD Item 2 responder rate (≥4-point improvement from Baseline)
  - Percent improvement in sweat production from Baseline
  - Proportion of patients with ≥50% reduction in sweat production from Baseline)
  - HDSS responder rate (≥2-grade improvement from Baseline)
  - Change in DLQI

RESULTS

Disposition, Demographics, and Baseline Disease Characteristics

- In ATMOS-1 and ATMOS-2, approximately 350 patients were randomized in each trial, and >90% completed Week 4 (**Figure 1**)
- Patient demographics and Baseline characteristics were similar across trials and treatment arms; the GT group in ATMOS-1 had more variability in Baseline sweat production than the other treatment arms across studies (**Table 1**)

Figure 1. Patient Disposition



GT, topical glycopyrronium tosylate

Table 1. Patient Demographics and Baseline Disease Characteristics

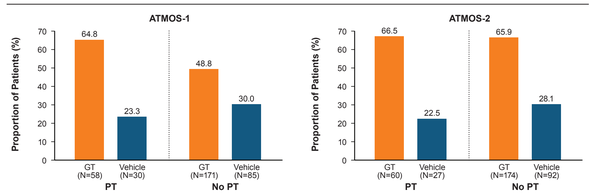
	ATMOS-1		ATMOS-2	
	Vehicle (N=115)	GT (N=229)	Vehicle (N=119)	GT (N=234)
Demographics				
Age (years), mean ± SD	34.0 ± 13.1	32.1 ± 11.2	32.8 ± 11.2	32.6 ± 10.9
Age group, n (%) ≥16 years	109 (94.8)	224 (97.8)	109 (91.6)	223 (95.3)
Male, n (%)	55 (47.8)	99 (43.2)	59 (49.6)	113 (48.3)
White, n (%)	94 (81.7)	182 (79.5)	102 (85.7)	192 (82.1)
Baseline Disease Characteristics				
Sweat production (mg/5 min), mean ± SD	170.3 ± 164.2	182.9 ± 266.9	181.9 ± 160.1	162.3 ± 149.5
ASDD Item 2 (sweating severity), mean ± SD	7.1 ± 1.7	7.3 ± 1.6	7.2 ± 1.6	7.3 ± 1.6
HDSS, n (%) Grade 3 Grade 4	84 (73.0) 31 (27.0)	133 (58.1) 96 (41.9)	71 (59.7) 47 (39.5)	144 (61.5) 90 (38.5)
DLQI,[a] mean ± SD	10.1 ± 5.9	12.1 ± 6.5	11.2 ± 5.8	11.6 ± 5.7
Prior treatments for hyperhidrosis,[b] n (%)	30 (26.1)	58 (25.3)	27 (22.7)	60 (25.6)

[a]Based on patients ≥16 years of age
[b]Includes botulinum toxin, oral/topical anticholinergics, and iontophoresis
ASDD, Axillary Sweating Daily Diary; BMI, body mass index; DLQI, Dermatology Life Quality Index; GT, topical glycopyrronium tosylate; HDSS: Hyperhidrosis Disease Severity Scale; ITT, intent-to-treat; SD, standard deviation

Prior Treatment Subgroup Analysis

- In each trial, a greater proportion of patients receiving GT were ASDD/ASDD-C Item 2 responders (reduced severity) compared to vehicle for both PT and No PT at Week 4 (**Figure 2**)

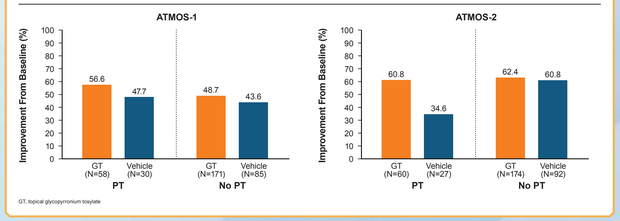
Figure 2. ASDD/ASDD-C Item 2 Responder Rate[a] at Week 4 According to Prior Treatment



[a]≥4-point improvement from Baseline
ASDD; Axillary Sweating Daily Diary; ASDD-C, Child-specific ASDD for patients <16 years of age; GT, topical glycopyrronium tosylate

- Mean decrease in sweat production (mg/5 min) was greater in the GT group versus the vehicle group for both PT and No PT in each trial (**Figure 3**)

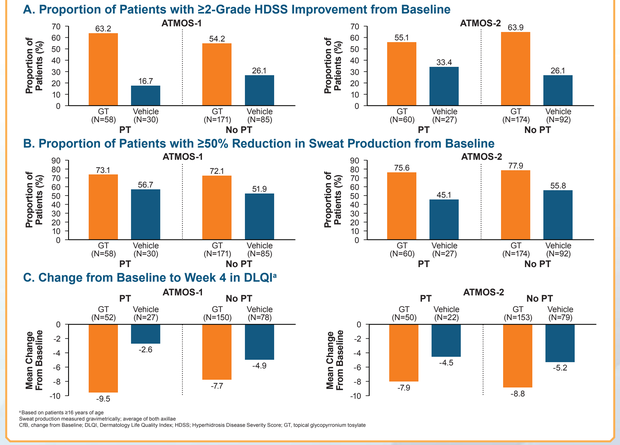
Figure 3. Percent Improvement From Baseline in Sweat Production at Week 4 According to Prior Treatment



GT, topical glycopyrronium tosylate

- Consistent benefits of GT over vehicle were observed for HDSS responder rate, sweat production responder rate, and change in DLQI at Week 4 regardless of prior treatment (**Figure 4**)

Figure 4. Additional Efficacy Endpoints at Week 4 According to Prior Treatment



[a]Based on patients ≥16 years of age
Sweat production measured gravimetrically; average of both axillae
CfB, change from Baseline; DLQI, Dermatology Life Quality Index; HDSS; Hyperhidrosis Disease Severity Score; GT, topical glycopyrronium tosylate

Safety

- In both trials, most TEAEs were mild or moderate, transitory, and infrequently led to discontinuation (ATMOS-1: 3.5% GT vs. 0.9% vehicle; ATMOS-2: 3.9% GT vs. 0% vehicle)
- In both trials, the majority of TEAEs in the GT group were related to anticholinergic activity, most frequently dry mouth: 18.9% GT vs 3.5% vehicle (ATMOS-1), 29.3% GT vs 7.6% vehicle (ATMOS-2)
- Two serious TEAEs were reported in GT-treated patients (moderate unilateral mydriasis [ATMOS-1; considered by the Investigator to be related to treatment]; moderate dehydration [ATMOS-2; considered by the Investigator to be unrelated to treatment])

CONCLUSIONS

- The efficacy results observed in this post hoc analysis of prior treatment subgroups are consistent with the overall efficacy results of the ATMOS-1 and ATMOS-2 trials, indicating that patients received clinically meaningful benefit from GT, as measured by reduction in sweat and improvement in perception of sweating severity, whether they were treatment naïve or had received prior treatment for axillary hyperhidrosis
- The majority of patients (~75%) were treatment naïve (self-reported) at Baseline in ATMOS-1 and ATMOS-2, suggesting that many patients may not seek or receive treatment for hyperhidrosis
- Topical glycopyrronium tosylate may provide noninvasive treatment for primary axillary hyperhidrosis

References

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Disclosures

DMP: Consultant and Investigator for Dermira, Inc. **AAH:** Consultant for Dermira, Inc.; employee of the University of Texas Medical School, Houston, which received compensation from Dermira, Inc. for study participation. **AN:** Employee of Charité – Universitätsmedizin Berlin, which received compensation from Dermira, Inc. for study participation. **WPW:** Consultant and investigator for Dermira. **SS:** Investigator for Dermira, Inc. **LG:** Investigator for Brickell; Advisory Board member and investigator for Dermira. **RDM:** Consultant for Dermira, Inc. **JQ:** Employee of QST Consultations. **JD:** Employee of Dermira, Inc. **DAG:** Consultant and Investigator for Dermira, Inc.

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