Burden of Axillary Hyperhidrosis Using a Patient-Reported Outcome Measure to Assess Impact on Activities and Bothersomeness

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INTRODUCTION

- Hyperhidrosis, which is estimated to affect 4.8% of the US population or approximately 15.3 million people, is associated with considerable impairment in work productivity, social activities, emotional well-being, and personal relationships[1,2]
- Topical glycopyrronium tosylate (GT; formerly DRM04), a cholinergic receptor antagonist, has been assessed in 2 replicate randomized phase 3 clinical trials (ATMOS-1 and ATMOS-2) for the treatment of primary axillary hyperhidrosis in patients ≥9 years of age; the primary efficacy and safety results of these studies have been previously reported[3]
- Patient-reported outcomes (PROs) from these pivotal trials were also assessed using the 4-item Axillary Sweating Daily Diary (ASDD),[4] 6 Weekly Impact items, and the single-item Patient Global Impression of Change (PGIC), that were developed according to current regulatory standards

OBJECTIVE

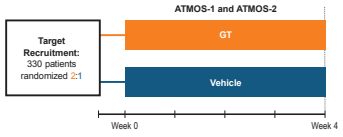
- To evaluate the burden of disease associated with primary axillary hyperhidrosis utilizing PRO measures reported at Baseline for patients who participated in ATMOS-1 and ATMOS-2

METHODS

ATMOS-1 and ATMOS-2 Study Design

- ATMOS-1 (NCT02530281; sites in the US and Germany) and ATMOS-2 (NCT02530294; US sites only) were parallel-group, 4-week, double-blind, phase 3 clinical trials in which patients with primary axillary hyperhidrosis were randomized (2:1) to GT or vehicle (**Figure 1**)
- For the purposes of this analysis, data from the GT and vehicle groups from each study have been pooled
- Eligible patients were ≥9 years of age and had primary axillary hyperhidrosis for ≥6 months, with gravimetrically-measured sweat production of ≥50 mg/5 min in each axilla, ASDD axillary sweating severity item (Item 2) score ≥4, and Hyperhidrosis Disease Severity Scale (HDSS) grade 3 or 4
- Patients were excluded for history of a condition that could cause secondary hyperhidrosis; prior surgical procedure or treatment with a medical device for axillary hyperhidrosis; treatment with iontophoresis within 4 weeks or treatment with botulinum toxin for axillary hyperhidrosis within 1 year; axillary use of nonprescription antiperspirant within 1 week or prescription antiperspirant within 2 weeks; new or modified psychotherapeutic medication regimen within 2 weeks; treatment with medications having systemic anticholinergic activity, centrally acting alpha-2 adrenergic agonists, or beta-blockers within 4 weeks unless dose had been stable ≥4 months and was not expected to change; and/or conditions that could be exacerbated by study medication

Figure 1. Study Design



Burden of Disease Measures

- Axillary Hyperhidrosis Patient Measures (AHPM)
  - The ASDD consists of 4 items and was used for patients ≥16 years; patients <16 years of age completed a modified, child-specific, 2-item version called the ASDD-C (**Table 1**)
  - Patients ≥16 years were additionally asked to complete 6 Weekly Impact items and a single-item Patient Global Impression of Change (PGIC; **Table 1**)
- The burden of disease associated with primary axillary hyperhidrosis was summarized by descriptive statistics in the intent-to-treat (ITT) population (all randomized subjects who were dispensed study drug) based on:
  - Mean score at Baseline on ASDD axillary sweating severity item (Item 2; all patients) and items addressing the impact and bother of sweating (Items 3 and 4, respectively; patients ≥16 years of age); Baseline was defined as the average of ≥4 days of data in the most recent 7 days prior to randomization
  - Mean score at Baseline for Weekly Impact items (patients ≥16 years of age); Baseline was defined as the last available record prior to Day 1
- An additional analysis was performed to assess the proportion of patients with moderate-to-severe axillary sweating, impact, and bother, defined as scores of 9 or 10 on ASDD Item 2 and scores of 3 or 4 on ASDD Items 3 and 4, respectively

Table 1. Axillary Hyperhidrosis Patient Measures (AHPM)[a]

Axillary Sweating Daily Diary (ASDD)[b]	
Instructions: The questions in the diary are designed to measure the severity and impact of any underarm sweating you have experienced within the previous 24 hour period, including nighttime hours. While you may also experience sweating in other locations on your body, please be sure to think only about your underarm sweating when answering these questions. Please complete the diary each evening before you go to sleep.	
Item 1 [Gatekeeper]	**During the past 24 hours**, did you have **any** underarm sweating? *Yes/No* When Item 1 is answered "no," Item 2 is skipped and scored as zero
Item 2	**During the past 24 hours**, how would you rate your underarm sweating **at its worst**? *0 (no sweating at all) to 10 (worst possible sweating)*
Item 3	**During the past 24 hours**, to what extent did your underarm sweating impact your activities? *0 (not at all), 1 (a little bit), 2 (a moderate amount), 3 (a great deal), 4 (an extreme amount)*
Item 4	**During the past 24 hours**, how bothered were you by your underarm sweating? *0 (not at all bothered), 1 (a little bothered), 2 (moderately bothered), 3 (very bothered), 4 (extremely bothered)*
Axillary Sweating Daily Diary-Children (ASDD-C)[c]	
Instructions: These questions measure how bad your underarm sweating was last night and today. Please think only about your underarm sweating when answering these questions. Please complete these questions each night before you go to sleep.	
Item 1 [Gatekeeper]	Thinking about **last night and today**, did you have any underarm sweating? *Yes/No* When Item 1 is answered "no," Item 2 is skipped and scored as zero
Item 2	Thinking about **last night and today**, how bad was your underarm sweating? *0 (no sweating at all) to 10 (worst possible sweating)*
Weekly Impact Items[b]	
Instructions: Please respond "Yes" or "No" to each of the following questions.	
a. **During the past 7 days**, did you ever have to change your shirt during the day because of your underarm sweating?	Yes/No
b. **During the past 7 days**, did you ever have to take more than 1 shower or bath a day because of your underarm sweating?	Yes/No
c. **During the past 7 days**, did you ever feel less confident in yourself because of your underarm sweating?	Yes/No
d. **During the past 7 days**, did you ever feel embarrassed by your underarm sweating?	Yes/No
e. **During the past 7 days**, did you ever avoid interactions with other people because of your underarm sweating?	Yes/No
f. **During the past 7 days**, did your underarm sweating ever keep you from doing an activity you wanted or needed to do?	Yes/No
Patient Global Impression of Change (PGIC) Item[b]	
Overall, how would you rate your underarm sweating **now** as compared to before starting the study treatment? *1 (much better), 2 (moderately better), 3 (a little better), 4 (no difference), 5 (a little worse), 6 (moderately worse), 7 (much worse)*	

[a]ASDD/ASDD-C Item 2 is a validated PRO measure
[b]For use in patients ≥16 years of age
[c]For use in patients ≥9 to < 16 years of age

RESULTS

- A total of 697 patients were randomized and were asked to complete ASDD/ASDD-C Items 1 and 2; 665 patients were ≥16 years of age and were asked to complete items addressing the impact and bother of sweating (Items 3 and 4, respectively), and the Weekly Impact items
- Demographics and Baseline disease characteristics were similar between studies (**Table 2**)

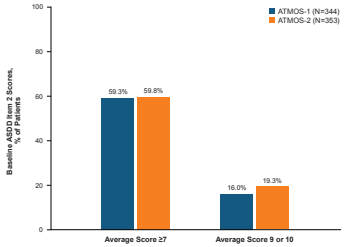
Table 2. Baseline Demographic and Disease Characteristics (ITT Populations)

	ATMOS-1 (N=344)	ATMOS-2 (N=353)
Demographics		
Age (years), mean ± SD	32.7 ± 11.9	32.6 ±11.0
Age group, n (%) <16 years ≥16 years	11 (3.2) 333 (96.8)	21 (5.9) 332 (94.1)
Male, n (%)	154 (44.8)	172 (48.7)
White, n (%)	276 (80.2)	294 (83.3)
BMI (kg/m²), mean ± SD	27.5 ± 5.5	27.7 ± 5.2
Baseline Disease Characteristics		
Years with primary axillary hyperhidrosis, mean ± SD	14.5 ± 10.7	16.5 ±10.7
Sweat production (mg/5 min)[a], mean ± SD	178.7 ± 237.4	168.9 ± 153.2
HDSS[b], n (%) Grade 3 Grade 4	217 (63.1) 127 (36.9)	215 (60.9) 137 (38.8)
ASDD Item 2[c], mean ± SD	7.2 ± 1.7	7.3 ± 1.6

[a]Gravimetrically measured
[b]HDSS grade 3 or 4 was an inclusion criteria for the study
[c]Average of daily records from the 7 days prior to date of first dose; a minimum of 4 days was required to compute the average
ASDD, Axillary Sweating Daily Diary; BMI, body mass index; HDSS, Hyperhidrosis Disease Severity Score; ITT, intent-to-treat

- At Baseline in ATMOS-1 and ATMOS-2, the mean ± SD ASDD/ASDD-C axillary sweating severity item (Item 2) scores were 7.2 ± 1.6 and 7.3 ± 1.6, respectively
  - In each trial, more than half of all patients reported weekly average scores ≥7 before randomization, indicating that patients considered their sweating to be moderate or severe at Baseline (**Figure 2**)
  - 16.0% and 19.3% of patients rated the severity of their axillary sweating as 9 or 10 in ATMOS-1 and ATMOS-2, respectively, indicating severe axillary hyperhidrosis at Baseline (**Figure 2**)

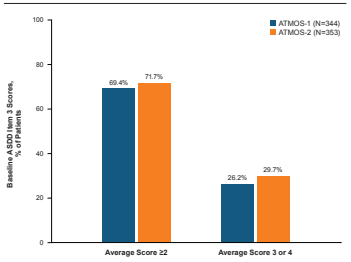
Figure 2. Proportion of Patients Reporting Moderate-to-Severe Axillary Sweating at Baseline (ASDD/ASDD-C Item 2 Scores)



Data are representative of the intent-to-treat (ITT) population
ASDD Item 2: **During the past 24 hours**, how would you rate your underarm sweating **at its worst**? *0 (no sweating at all) to 10 (worst possible sweating)*
ASDD-C Item 2: Thinking about **last night and today**, how bad was your underarm sweating? *0 (no sweating at all) to 10 (worst possible sweating)*
ASDD, Axillary Sweating Daily Diary; ASDD-C, ASDD-Children

- At Baseline in ATMOS-1 and ATMOS-2, mean ± SD ASDD Item 3 (impact of axillary sweating) scores were 2.3 ± 0.9 and 2.4 ± 0.9, respectively
  - In each trial, approximately 70% of patients ≥16 years of age reported scores ≥2 on ASDD Item 3, indicating that their daily activities were at least moderately affected by axillary hyperhidrosis at Baseline (**Figure 3**)
  - 26.2% and 29.7% of patients were severely impacted by axillary sweating in ATMOS-1 and ATMOS-2, respectively, having reported scores of 3 or 4 at Baseline (**Figure 3**)

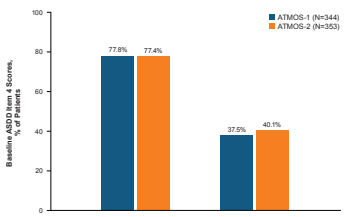
Figure 3. Proportion of Patients Reporting Moderate-to-Severe Impact of Axillary Sweating at Baseline (ASDD Item 3 Scores)



Data are representative of the intent-to-treat (ITT) population
ASDD Item 3: **During the past 24 hours**, to what extent did your underarm sweating impact your activities? *0 (not at all), 1 (a little bit), 2 (a moderate amount), 3 (a great deal), 4 (an extreme amount)*
ASDD, Axillary Sweating Daily Diary

- At Baseline in ATMOS-1 and ATMOS-2, the mean ± SD ASDD Item 4 (bother of axillary sweating) scores were 2.6 ± 0.9 and 2.6 ± 0.9, respectively
  - In each trial, >75% of patients ≥16 years of age reported scores ≥2 on ASDD Item 4, indicating that they were at least moderately bothered by axillary sweating at Baseline (**Figure 4**)
  - 37.5% and 40.1% of patients were severely bothered by axillary sweating in ATMOS-1 and ATMOS-2, respectively, having reported scores of 3 or 4 at Baseline (**Figure 4**)

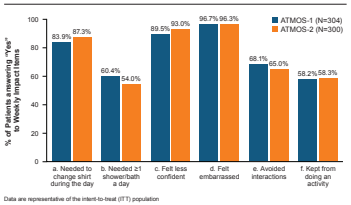
Figure 4. Proportion of Patients Reporting Moderate-to-Severe Bother of Axillary Sweating at Baseline (ASDD Item 4 Scores)



Data are representative of the intent-to-treat (ITT) population
ASDD Item 4: **During the past 24 hours**, how bothered were you by your underarm sweating? *0 (not at all bothered), 1 (a little bothered), 2 (moderately bothered), 3 (very bothered), 4 (extremely bothered)*
ASDD, Axillary Sweating Daily Diary

- At Baseline, the majority of patients who were ≥16 years of age answered 'yes' to questions asking if their underarm sweating affected their actions or emotions (Weekly Impact Items) during the past week (**Figure 5**)
  - Notably, more than 96% of patients reporting feeling embarrassed

Figure 5. Proportion of Patients Answering 'Yes' to Weekly Impact Items



Data are representative of the intent-to-treat (ITT) population

CONCLUSIONS

- At Baseline, more than half of all patients who participated in ATMOS-1 and ATMOS-2 reported that their sweating was at least a 7 on an 11-point scale where 0 represents no sweating and 10 represents worst possible sweating
- In patients who were ≥16 years of age, axillary hyperhidrosis at least moderately affected their daily activities and was considered at least moderately bothersome
  - Approximately 1 in 5 patients reported experiencing severe axillary sweating
  - Approximately 1 in 3 reported feeling severely impacted and/or bothered by their sweating
- On a weekly basis, the majority of patients who were ≥16 years of age reported being markedly impacted by their excess sweating, with most having to avoid interactions or take additional measures (ie, showering/bathing more than once a day; changing shirts during the day) to manage their excessive sweating; more than 90% of patients were less confident or embarrassed by sweating
- These findings are consistent with previous reports that hyperhidrosis is associated with a substantial disease burden; as such, safe and effective new treatment options are needed for this disease

References

1. Doolittle et al. *Arch Dermatol Res.* 2016; 308 (10):743-9. 2. Hamm. *Dermatology.* 2006;212:343-53. 3. Pariser et al. Poster presented at: the 25th European Academy of Dermatology and Venereology Congress; September 28–October 2, 2016; Vienna, Austria. 4. Pariser et al. Poster presented at: 13th Annual Maui Derm for Dermatologists; March 20-24, 2017; Maui, HI.

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