INTRODUCTION

• Hyperhidrosis affects an estimated 4.8% of the US population,1 approximately three-quarters of patients experience negative psychological effects, with anxiety and depression occurring over 3-5 times more frequently in people with hyperhidrosis than in people without it.2

• Despite high prevalence and burden of disease, few disease-specific outcome measures are available.

• The Hyperhidrosis Disease Severity Scale (HDSS) is widely used in clinical studies and well understood in clinical practice; however, it does not conform to current regulatory standards for patient-reported outcome (PRO) measures used to support product approval and labeling.

• The 4-item Axillary Sweating Daily Diary (ASDD, Table 1) and a child-specific 2-item version (ASDD-C for use in patients ≥9 to <16 years of age; Table 1) were developed according to current regulatory standards.1,3

• The ASDD/ASDD-C axillary sweating severity item (Item 2) was specifically developed for use as an endpoint in clinical trials in support of approval and labeling (and also as a useful clinical parameter).

• In addition to the ASDD, patients ≥16 years of age were asked to complete 6 Weekly Impact Items designed to assess the impact and bother of hyperhidrosis on daily activities and a single-item Patient Global Impression of Change (PGIC) to assess overall change in sweating severity (Table 1).

• Initial psychometric evaluation of the ASDD was conducted using data from a phase 2 study of topical glycopyrronium tosylate (GT, formerly DR404), an investigational treatment for primary axillary hyperhidrosis in patients ≥25 years of age; results have been previously reported and provide preliminary support for the use of this measure to evaluate the efficacy of axillary hyperhidrosis treatment in clinical trials.1,3

OBJECTIVE

• To confirm and extend the psychometric evidence supporting ASDD/ASDD-C axillary sweating severity item (Item 2) based on pooled data from two phase 3 clinical trials of GT: ATMOS-1 (DRM4-HH04; NCT02530281) and ATMOS-2 (DRM4-HH05; NCT02530294).

METHODS

Study Design

• ATMOS-1 and ATMOS-2 were phase 3, multicenter (ATMOS-1: sites in US and Germany; ATMOS-2: sites in US), parallel-group, 4-week, double-blind clinical trials in which patients with primary axillary hyperhidrosis were randomized (2:1) to GT or vehicle.

• Eligible patients were ≥25 years of age (patients <16 years were only recruited at US sites) and had primary axillary hyperhidrosis for ≥6 months, with gravimetrically-measured sweat production of ≥50 mg/5 min in each axilla. ASDD/ASDD-C axillary sweating severity item (Item 2) score ≥4, and Hyperhidrosis Disease Severity Scale (HDSS) grade 3 or 4.

Assessments

• Axillary Hyperhidrosis Patient Measures (AHPM)

• ASDD/ASDD-C Item 2 response and sweat production were assessed in two age groups (≥25 years and ≥16 years)

• ASDD/ASDD-C Items were scored as a weekly average of daily responses; at least 4 days of daily data were required for analysis

• Weekly Impact Items and PGIC were included to evaluate construct validity

Psychometric Evaluation

• Potential floor and ceiling effects and nonresponse bias were evaluated based on both summary statistics and graphical techniques

• Test-retest reliability was evaluated through the computation of intraclass correlation coefficients (ICCs) between Week 3 and Week 4; a value ≥0.70 was considered acceptable

• Construct validity was evaluated at Week 4 based on correlations between ASDD/ASDD-C Item 2 and ASDD items related to the impact and bother of sweating (Items 3 and 4, respectively), HDSS, sweat production, and other PRO measures as available.

• All statistical tests were two-tailed using a type I error rate of 0.01 (% alpha=0.01)

Table 1. Axillary Hyperhidrosis Patient Measures (AHPM)

<table>
<thead>
<tr>
<th>Item</th>
<th>Instructions</th>
<th>Response Options</th>
<th>Rating</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>During the past 4 days, did you have any underarm sweating?</td>
<td>None</td>
<td>1</td>
<td>0-7</td>
</tr>
<tr>
<td>3</td>
<td>During the past 4 days, how would you rate your underarm sweating at its worst?</td>
<td>1 (not at all bothered), 2 (a little bothered), 3 (moderately bothered), 4 (very bothered), 5 (extremely bothered)</td>
<td>1-5</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>During the past 7 days, how much did your underarm sweating affect your daily activities?</td>
<td>None</td>
<td>1</td>
<td>0-7</td>
</tr>
</tbody>
</table>

RESULTS

• The response distribution for the ASDD/ASDD-C axillary sweating severity item (Item 2) demonstrated no floor or ceiling effect, and no nonresponse bias (Table 3).

• Construct validity was supported by strong correlations between ASDD Item 2 and the AHPM items addressing the impact and bother of axillary sweating (Items 3 and 4, respectively) (Table 3).

• Test-retest reliability was supported by ICCs of 0.53 for both age subgroups (Table 3), which is well above the 0.70 criterion, and within the confidence interval of the phase 2 estimate of 0.91 (95% CI: 0.87, 0.94).

• The ASDD/ASDD-C Item 2 responsiveness, or ability to detect change in sweating severity, was demonstrated by large effect sizes and correlations that were within the expected range for the change in ASDD/ASDD-C Item 2 and the change in the gravimetric measures of sweat production (Table 3).

CONCLUSIONS

• The current study confirms and extends the psychometric evidence supporting the ASDD/ASDD-C as a new PRO measure developed according to current regulatory standards.

• The psychometric findings presented here continue to support use of the ASDD/ASDD-C axillary sweating severity item (Item 2) as an endpoint in assessing the efficacy of treatments for patients with axillary hyperhidrosis.

References


Author Disclosures

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