Asthma Working Group
Presented at the Fifth Annual PRO Consortium Workshop – Silver Spring, MD – April 29-30, 2014

Background

Rationale for Asthma Working Group (WG)
• Asthma was defined as an area for development of novel PRO measures to support clinical trials. There is no standard PRO instrument that is qualified by the FDA for the purpose of measuring important patient-experienced aspects of asthma.
• The mission of the Asthma WG is to address this unmet need in close collaboration with regulatory agencies by evaluating and developing PRO instruments for use in clinical trials of asthma therapies in accordance with the FDA PRO Guidance.

Goal of the Asthma WG
• To develop a patient-reported daily diary to document daily asthma symptoms

Milestones

Overall
Patients treated with [drug X] reported significant reduction in asthma symptom severity

Daytime Symptoms
Patients treated with [drug X] reported significant reduction in daytime asthma symptom severity
Patients treated with [drug X] reported significantly fewer days with asthma symptoms

Nighttime Symptoms
Patients treated with [drug X] reported significant reduction in nighttime asthma symptom severity
Patients treated with [drug X] reported significantly fewer nights of awakenings due to asthma symptoms.

Individual Symptoms
[drug X] reduces severity of wheezing / difficulty breathing / shortness of breath / cough

Content of Interest

Endpoint Model for Treatment of Asthma

<table>
<thead>
<tr>
<th>Endpoint Category</th>
<th>Endpoint Concept(s)</th>
<th>Type of Endpoint</th>
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</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Improvements in airflow re-obstruction</td>
<td>COA (PerFD)</td>
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<td></td>
<td>FEV1 Reduction in asthma symptoms</td>
<td>PRO</td>
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<td></td>
<td>Asthma symptom score from Asthma Daily Symptom Diary</td>
<td>PRO</td>
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<tr>
<td>Secondary</td>
<td>Daytime Symptoms</td>
<td>PRO</td>
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<td></td>
<td>Proportion of days without symptoms based on Asthma Daily Symptom Diary</td>
<td>PRO</td>
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<td></td>
<td>Nighttime Symptoms</td>
<td>PRO</td>
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<td>Proportion of nights without asthma symptoms based on Asthma Daily Symptom Diary</td>
<td>PRO</td>
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Target Population
• Adolescents and adults aged 12 years and older, with a clinical diagnosis of asthma with lung function impairment
• Patients will be categorized in the guideline-defined levels of disease severity, which include mild through severe persistent asthma (GINA, 2009).

Revised Hypothesized Conceptual Framework*

Core Asthma Symptoms (Assessed for Daytime & Nighttime)

- Difficulty breathing
- Wheezing
- Shortness of breath
- Chest tightness
- Chest pain
- Pressure/weight on chest
- Cough
- Mucus/phlegm

Other Measurement Concepts

- Nighttime awakenings
- Activity limitation
- Relief Medication Use

Validity

*Framework to be finalized after the completion of the quantitative study.

Draft Instrument

Core Items: Eight items were developed to measure the ‘core’ asthma symptoms identified during concept elicitation. Three additional items were developed to measure other concepts related to asthma (i.e., nighttime awakenings, activity limitations, relief inhaler use)

Recall Period: Twice daily (morning and evening)

Response Options: Respondents asked to rate each symptom at its ‘worst’ using a 0-10 numeric rating scale, which is consistent with patients’ spontaneous descriptions of symptom severity

Symptom Attribute: Severity was chosen (as opposed to frequency, duration, or bothersomeness) based on patient descriptions of asthma symptom experience

Updates

• Completed rounds 1 and 2 of cognitive interviews
• The FDA provided positive feedback to the November 2013 submission of qualitative research through round 1 cognitive interviews and the draft instrument
• CRC Health, the selected ePRO system provider, implemented the instrument on a demo handheld device for rounds 2 and 3 of cognitive interviews
• Round 3 of cognitive interviews completed March 3-13, 2014
• Results to be reviewed with expert panel members at a face-to-face meeting May 1, 2014.

Working Group Plans

Next Steps
• FDA submission to include the qualitative research updates from completion of cognitive interviews , the revised instrument, and the quantitative research protocol (target June 2014)
• Sponsor project agreement amendments initated
• The quantitative component of the Content Validity Stage will commence once nine sponsor agreement amendments are fully executed and FDA feedback has been received regarding the study protocol

Dissemination Plan
• AIS – May 2014
• Poster on the concept elicitation and item generation process
• Poster on the qualitative literature and instrument review
• Manuscript on qualitative research methodology and results

Working Group Participants

Company/Organization
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