Pediatric Asthma Working Group

Presented at the Eighth Annual PRO Consortium Workshop – Bethesda, MD – April 26-27, 2017

PRO CONSORTIUM
CRITICAL PATH INSTITUTE

Background

Rationale for Pediatric Asthma Working Group (WG)

- Pediatric asthma has been identified as an area in need of novel clinical outcome assessment (COA) tools for evaluating treatment benefit in clinical trials.
- The Asthma Working Group (WG) is developing a patient-reported outcome (PRO) measure (i.e., *Asthma Daily Symptom Diary* [*ADSD*]) for assessing asthma symptom severity in adolescents and adults. The U.S. Food and Drug Administration (FDA) requested that the Asthma WG consider developing COA tools to cover a broader range of asthma patients (i.e., < 12 years old).
- Merck, a sponsor of the Asthma WG, contributed draft versions of a PRO measure (for completion by children ages 8-11 years) and an observer-reported outcome (ObsRO) measure (for completion by parents of children ages 4-11 years) developed for use in pediatric asthma trials.
- The Asthma WG decided to focus its efforts on FDA qualification of the *ADSD,* so a separate Pediatric Asthma WG was formed to examine Merck's research and assess the adequacy of the two draft questionnaires.

Goal of the Pediatric Asthma WG

- To pursue FDA qualification of a COA measure that would be completed by the parent and child together, involving interview administration, with the parent sitting with the child and talking through the questions and answers with the child. The parent would also consider input from other informants (e.g., siblings, teachers, babysitters, spouses) regarding observable asthma signs or impacts.

Targeted Labeling Language

- Patients treated with [Product X] experienced a significant reduction in severity of asthma signs and symptoms.

Milestones

Milestone	Target Date	Completed Date
Reanalysis of Merck's qualitative data to evaluate data and identify gaps suggested by FDA that required additional research.		SEP 2016
Letter of Intent submitted to FDA		DEC 2016
Phase I: Review of documentation, recommendations for changes to the measure and recommendations for future research		FEB 2017
Phase 2: Additional qualitative research and feasibility study	TBD	
Submit Qualitative Research Summary Briefing Document to FDA for review and feedback	TBD	
Complete quantitative pilot study (if needed)	TBD	
Complete documentation of content validity and cross-sectional evaluation of other measurement properties	TBD	
Submit Qualification Briefing Package to FDA for use of the novel COA tool as an exploratory endpoint measure	TBD	

Highlights

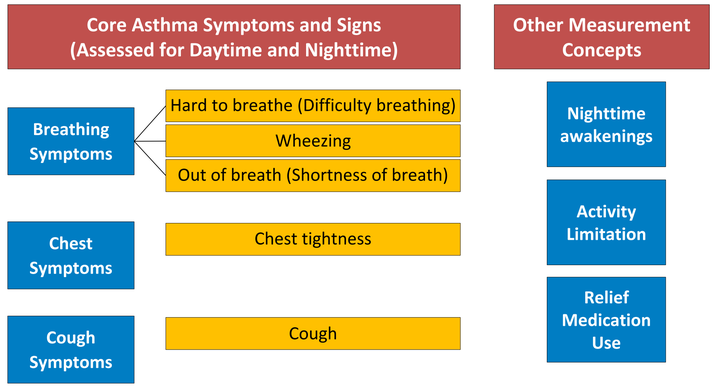
Example Endpoint Model for Treatment of Pediatric Asthma

Endpoint Hierarchy	Endpoint Concept(s)	Endpoint Type
Primary	Improvements in airflow obstruction • FEV1 Reduction in asthma symptoms and signs • Total asthma severity score from measure (TBD)	PerfO Hybrid PRO/ObsRO
Secondary	Daytime Symptoms – Symptom Free Days Proportion of days without asthma symptoms or signs based on measure (TBD) Night-time Symptoms – Symptom Free Nights Proportion of nights without asthma symptoms or signs based on measure (TBD)	Hybrid PRO/ObsRO Hybrid PRO/ObsRO

Target Population

- Children 4 to 11 years old with a clinical diagnosis of mild to severe persistent asthma requiring a daily long-term control medication

Hypothesized Conceptual Framework



Draft Measure – Hybrid, co-completed measure proposed

- Concerns about complete and consistent coverage of asthma symptoms across ages using separate ObsRO and PRO measures led to consideration of a co-completed model
- Recommendations for a measure and measurement approach (i.e., co-completion) are being considered, along with options and a "plan B" to pursue in the event that the feasibility study shows that co-completion of the measure does not allow the child's voice to be heard.
- Instructions have been drafted for the parent to follow when completing the measure with his or her child in order to standardize the co-completion process across respondents.

Working Group Updates

Unique Issues for the Working Group

- The age range for this target population is particularly challenging because of the wide range in cognitive development, ability to reliably report symptoms and understand timeframes (e.g., last night; since you woke up this morning), and ability to read and understand the diary questions.
- In addition, asthma is a symptomatic condition for which key symptoms such as chest tightness are not easily observed by others and therefore rely heavily on self-report.
- The approach used in the Merck research, where children 8 to 11 complete a PRO questionnaire on their own, while parents completed an ObsRO questionnaire for all ages, was determined to be problematic because of the limitations of observability of nighttime symptoms (as parents would also be sleeping) and of daytime symptoms (because parents may not be with the child for enough time during the day to reliably report their observations).
- The Pediatric Asthma WG decided to pursue a hybrid or dyad approach to address these limitations, as it would enable both perspectives to contribute to the responses selected, with the parent providing more input for the younger children who may not report as reliably and the parent using interviewer-administration for the older children who are better able to self-report.
- Concerns remain about the ability of the parent to accept the child's response without overriding it; this will be evaluated in a feasibility study.
- Questions regarding how best to incorporate input from other informants (e.g., siblings, teachers, babysitters, spouses) regarding observable asthma signs and impacts.

Next Steps

- If FDA agrees that this initiative can enter the qualification program, modify measure and prepare for use as a hybrid measure that is co-completed by child and parent (or primary caregiver).
- Provided WG supports moving forward, issue an RFP for the additional qualitative and quantitative research:
  - Cognitive interviewing of modified measure
  - Feasibility study (added to cognitive interview study)
- Consider alternatives for assessing sleep/night-time awakenings (e.g., wearables)

Working Group Participants

Company/Organization	Representatives
AstraZeneca AB	Sean O'Quinn, MPH
GlaxoSmithKline , LLC	Linda Nelsen, MHS
Novartis Pharma AG	Dorothy Keininger, MS; Jessica Marvel, MPH
Affiliation	**Consultant**
Patient-Centred Outcomes Assessments, Ltd. (P-COA)	Linda Abetz-Webb