Asthma Working Group

Presented at the Ninth Annual PRO Consortium Workshop – Silver Spring, MD – April 25-26, 2018

PRO CONSORTIUM CRITICAL PATH INSTITUTE

Background

Rationale for Asthma Working Group (WG)

- Asthma was identified as an area for development of a novel PRO measure to support clinical trials. There is no standard PRO instrument that is qualified by the FDA for the purpose of measuring important symptoms of asthma.
- The Asthma WG is working to address this unmet need within FDA's COA Qualification Program by developing a PRO instrument 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 diary to document daily asthma symptoms in adults and adolescents with a clinical diagnosis of mild to severe persistent asthma for use in clinical trials of asthma therapies as a co-primary or secondary endpoint measure to establish treatment benefit

Targeted Labeling Language

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
Night-time Symptoms	• Patients treated with [*Drug X*] reported significant reduction in night-time asthma symptom severity • Patients treated with [*Drug X*] reported significantly fewer nights of awakenings due to asthma symptoms

Milestones

Milestone	Expected Date	Completed Date
Vendor selection and contracting		FEB 2012
Complete background research (Literature Review Report and Expert Panel Meeting)		SEP 2012
Draft Instrument: Complete initial qualitative research and generate items (concept elicitation interviews, item generation, expert panel input, and initial round of cognitive interviews)		AUG 2013
Submit Qualitative Research Summary Briefing Document to FDA for review and feedback		NOV 2013
Complete quantitative pilot study		OCT 2015
Complete data analysis and Quantitative Pilot Study Report		OCT 2016
Submit Qualification Briefing Package to FDA for exploratory use of *ADSD*		DEC 2016
Complete revised Quantitative Pilot Study Report incorporating reanalysis of ADSD with 6 instead of 7 items (mucus/phlegm item removed at FDA request)		OCT 2017
Submit revised Qualification Briefing Package for 6-item *ADSD*	MAY 2018	

Highlights

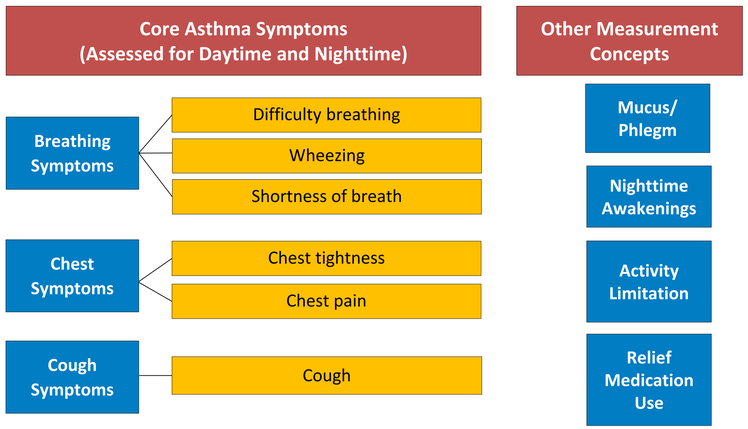
Example Endpoint Model for Treatment of Asthma

Endpoint Hierarchy	Endpoint Concept(s)	Endpoint Type
Primary	Improvements in airflow obstruction • FEV_1 Reduction in asthma symptoms • Asthma symptom scores from *Asthma Daily Symptom Diary* (*ADSD*)	PerfO PRO – *ADSD*
Secondary	Daytime Symptoms • Proportion of days without symptoms based on *Asthma Daily Symptom Diary* (symptom free days) Night-time Symptoms • Proportion of nights without asthma symptoms based on *Asthma Daily Symptom Diary*	PRO PRO

Target Population

- Adolescents and adults aged 12 years and older with a clinical diagnosis of asthma with lung function impairment
- Patients across guideline-defined levels of disease severity, which include mild through severe persistent asthma (GINA, 2009)

Conceptual Framework



Measure – *Asthma Daily Symptom Diary* (*ADSD*)

Core Items: Six items assessing three symptom domains
Note: Five supplementary items assess attributes related to asthma (mucus/phlegm, nighttime awakenings, activity limitations, relief inhaler use, nebulizer use) for optional use in clinical trials.
Recall Period: Twice daily (morning and evening)
Response Options: 11-point numeric rating scale
Symptom Attribute: Severity was chosen (as opposed to frequency, duration, or bothersomeness) based on patient descriptions of asthma symptom experience.
Data Collection Mode: Handheld smartphone device used for quantitative pilot study

Working Group Updates

Completed Activities

- Quantitative Pilot Study Report and quantitative data submitted to FDA in October 2016
- Qualification Briefing Package submitted to FDA in December 2016
- At FDA request, mucus/phlegm item removed and reanalysis performed on 6-item measure
- Revised Quantitative Pilot Study Report reflecting 6-item measure analysis submitted to FDA in October 2017
- Revised Qualification Briefing Package submitted to FDA in April 2018

Information Dissemination

- Gater A, Nelsen L, Fleming S, et al. Assessing asthma symptoms in adolescents and adults: Qualitative research supporting development of the Asthma Daily Symptom Diary. *Value in Health* 2016;19(4): 440-450.
- Two posters were presented at the American Thoracic Society International Conference on May 22, 2017 in Washington, DC:
  - Preliminary psychometric evaluation of the *Asthma Daily Symptom Diary* (*ADSD*)
  - Respondent understanding and user experience with the *Asthma Daily Symptom Diary* (*ADSD*), a novel patient-reported outcome measure
- A manuscript reporting the results of the quantitative pilot study will be prepared for submission to *Chest* following qualification of the *ADSD* for exploratory use

Unique Issues

- The Item Refinement Meeting held in January 2016 resulted in a 7-item measure that was agreed to by WG, Expert Panel, and FDA representatives, and quantitative analysis was conducted accordingly
- In April 2017, FDA requested the Asthma WG to drop one of the 7 items of the *ADSD*, conduct reanalysis with the resulting 6-item measure and resubmit a revised Quantitative Pilot Study Report, and subsequently a revised Qualification Briefing Package

Working Group Participants

Company/Organization	Representatives
AstraZeneca AB	Niklas Karlsson, PhD; Sean O'Quinn
Boehringer Ingelheim	Mike Baldwin, MBA
Allergan	Robyn T. Carson, MPH
Genentech, Inc.	Alison Greene, MPH; Alison Matsui, MPH
GlaxoSmithKline , LLC	Linda Nelsen, MHS (Co-Chair)
Janssen Global Services, LLC	Chenglong Han, MD, PhD
Merck Sharp & Dohme Corp.	Josephine Norquist, MS
Novartis Pharma AG	Luísa Álvares, MPharm; Jessica Marvel, MPH
Pfizer, Inc.	Sheryl Pease, MBA, PMP
Sanofi	Asif Khan; Lauren Eckert
Expert Panel Members	**Affiliation**
Michael Schatz, MD	Kaiser Permanente, UCSD
Jerry Krishnan, MD, PhD	University of Chicago, NHLBI
John Haughney, MB	University of Aberdeen
Stuart Stoloff, MD	Fellow FAAAAI, Family Practitioner
Contract Research Organization	**Research Team**
Adelphi Values	Adam Gater, MSc; Rob Arbuckle, MSc; Nicola Bonner, MSc; Rebecca Hall, MMedSci; Gemma Barrett; Hannah Saunton
ePRO System Provider	**Representative**
CRF Health	Paul O'Donohoe, BSc (at the time of the study)