Asthma Working Group

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

PRO CONSORTIUM CRITICAL PATH INSTITUTE

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 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 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
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

Milestones

Milestone	Expected Date	Completed Date
Scoping Stage	Mar2010	Nov2010
Content Validity Stage		
Vendor selection and contracting	Jun2011	Feb2012
Complete background research (Literature Review Report and Expert Panel Meeting)	Jul2012	Sep2012
Draft Instrument: Complete initial qualitative research and generate items (concept elicitation interviews, item generation, expert panel input, and initial round of cognitive interviews)	Aug2013	Aug2013
Submit Qualitative Research Summary Briefing Document to FDA for review and feedback	Oct2013	Nov2013
Submit updates to FDA for review and feedback (round 3 cognitive interviews, final cognitive interview report, expert panel meeting, updated instrument, and quantitative protocol)	Jun2014	
Complete documentation of content validity and cross-sectional evaluation of other measurement properties	2Q2015	
Submit exploratory endpoint qualification dossier to FDA	3Q2015	

Content of Interest

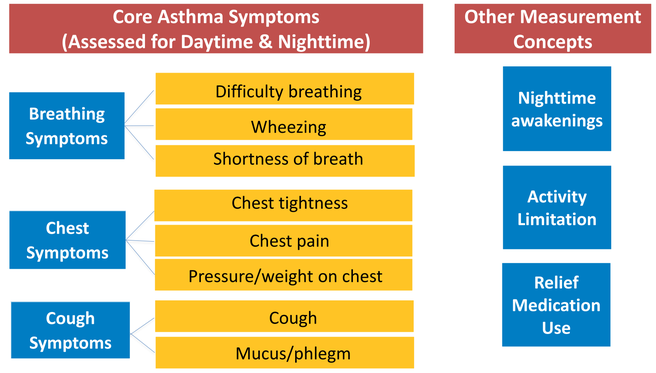
Endpoint Model for Treatment of Asthma

Endpoint Hierarchy	Endpoint Concept(s)	Type of Endpoint
Primary	Improvements in airflow re-obstruction • FEV1 Reduction in asthma symptoms • Asthma symptom score from Asthma Daily Symptom Diary	COA (PerfO) PRO
Secondary	Daytime Symptoms • Proportion of days without symptoms based on Asthma Daily Symptom Diary (symptom free days) Nighttime 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 will be categorized in the guideline-defined levels of disease severity, which include mild through severe persistent asthma (GINA, 2009).

Revised Hypothesized Conceptual Framework*



*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
- CRF 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 initiated
- 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

- ATS – 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	Name
Actelion Pharmaceuticals, Ltd.	Elke Hunsche
Amgen Inc.	Brian Ortmeier, Gary Globe
AstraZeneca AB	Niklas Karlsson, Sean O'Quinn
Boehringer Ingelheim	Dirk Esser, John Downie
Forest Research Institute, Inc.	Michelle Mocarski (co-chair)
Genentech, Inc.	Alison Greene, Kristina Fitzgerald
GlaxoSmithKline , LLC	Margaret Tabberer, Richard Stanford, Linda Nelsen (co-chair)
Ironwood Pharmaceuticals, Inc.	Brooke Witherspoon, Vineeta Belanger
Janssen Global Services, LLC	Sarah Fleming, Renee Pierson
Merck Sharp & Dohme Corp.	Scott Greenfeder, Josephine Norquist
Novartis Pharma AG	Karoly Kulich
Sanofi	Asif Khan
Expert Panel Members	**Affiliation**
Michael Schatz, M.D.	Kaiser Permanente, UCSD
Jerry Krishnan, M.D., PhD	University of Chicago, NHLBI
John Haughney, M.B.	University of Aberdeen
Stuart Stoloff, M.D.	Fellow FAAAAI, Family Practitioner

Contract Research Organization	Research Team
Adelphi Values	Adam Gater, Rob Arbuckle, Nicola Bonner, Chris Marshall, Rebecca Hall, Kerry Turner, Hannah Staunton