Asthma Working Group

Presented at the Fourth Annual PRO Consortium Workshop – Silver Spring, MD – April 24-25, 2013

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 [*drugX*] 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 [*drugX*] reported significantly fewer nights of awakenings due to asthma symptoms.
Individual Symptoms	[*drugX*] reduces severity of wheezing / difficulty breathing / shortness of breath / cough

Milestone	Expected Date	Completed Date
Scoping Stage	March 2010	November 2010
Content Validity Stage		
Vendor selection and contracting	June 2011	February 2012
Completion of background research (literature review and 1st expert panel)	July 2012	September 2012
Completion of initial qualitative research and generate items (concept elicitation, selection and item generation – patients interviews & expert panels)	November 2012	February 2013
Refining initial instrument (cognitive interviewing, final expert panel, identification of ePRO platform, translatability assessment)	October 2013	
Qualitative research briefing package/document submitted to FDA for interim review	January 2014	
Quantitative analysis	To be completed as a separate scope of work	
Content validity document submitted to FDA for interim review		
Psychometric Testing Stage	TBD	

Content of Interest

Endpoint Model for Treatment of Asthma

Endpoint Hierarchy	Endpoint Concept(s)	Clinical Outcome Assessment (COA) /Biomarker/ Survival
Primary	Improvements in airflow re-obstruction • FEV1	COA
	Reduction in asthma symptoms • Asthma symptom score from Asthma Symptom Diary	PRO
Secondary	Daytime Symptoms • Proportion of days without symptoms based on Asthma Symptom Diary (symptom free days)	PRO
	Nighttime Symptoms • Proportion of nights without asthma symptoms based on Asthma Symptom Diary	PRO

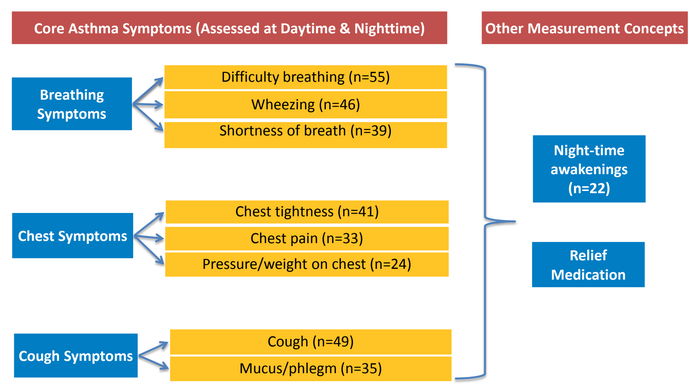
Target Population

- 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).

Updates

- The protocol and study documents were submitted to the FDA for consultation and advice with positive feedback.
- Concept elicitation interviews were conducted in southern, western, and eastern US sites, and concluded in January 2013 achieving full saturation. The population included 55 patients and met target samples for asthma control, age, ethnicity, sex, and education.
- Information from qualitative literature review and analysis of qualitative data contributed by Pfizer was used alongside results of the concept elicitation interviews to determine key measurement concepts.
- The Item Generation Meeting was held in February 2013 in Chicago, IL.
- The team is preparing the preliminary measure/draft instrument for the electronic implementation assessment, the translatability assessment, and cognitive interviewing.

Revised Hypothesized Conceptual Framework



Working Group Plans

Next Steps:

- Draft instrument
  - In-depth translatability assessment
  - Electronic Implementation Assessment by the ePRO Consortium
  - Working group to chose an electronic platform for electronic implementation
  - In-kind electronic implementation for use in cognitive interviews
  - Review and approval of ePRO screenshots
- Cognitive interviewing study protocol and interview guide
- Cognitive debriefing , final instrument and final report (Oct 2013)

Future Plans

- Plans for quantitative assessment
- Submission of qualitative research, draft diary and plans for quantitative research

Dissemination Plan

- ISOQOL 2014 – poster presenting the qualitative research findings
- ATS 2014 – presentation of the draft instrument including scaling and quantitative research objectives
- Manuscript detailing the qualitative research findings

Topics for Discussion

Lessons Learned

- With the conclusion of the item generation meeting, the WG now has made sufficient progress and has concrete information to discuss to request a teleconference with the FDA.
- Expert panelists involvement at all stages has been hugely beneficial. The experts have experience in PRO development and vital clinical knowledge, understand the qualitative research process, and have been very engaged and constructive to the item generation process.

Working Group Participants

Company/Organization	Name
Actelion Pharmaceuticals, Ltd.	Elke Hunsche
Amgen Inc.	Brian Ortmeier, Gary Globe
AstraZeneca AB	Niklas Karlsson
Boehringer Ingelheim	Michael Engel, Dirk Esser, John Downie
Forest Research Institute, Inc.	Michelle Mocarski, Stephanie Chen, Steven Blum, Paul Rowe
GlaxosmithKline LLC	Margaret Tabberer, Richard H. Stanford (co-chair)
Ironwood Pharmaceuticals, Inc.	Brooke Dennee-Sommers, Vineeta Belanger
Janssen Global Services, LLC	Sarah Fleming, Renee Pierson
Merck Sharp & Dohme Corp.	Linda Nelsen (co-chair), Scott Greenfeder
Novartis Pharma AG	Karoly Kulich
Genentech, Inc.	Alison Greene, Kristina Fitzgerald
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, Linda Abetz, Nicola Bonner, Chris Marshall, Rebecca Hall, Kerry Turner