Asthma Working Group

Presented at the Third Annual PRO Consortium Workshop – Silver Spring, MD – April 4, 2012

Background

Rationale for Asthma Working Group (WG)

- Asthma was defined as a priority area for development of novel PRO measures to support clinical trials. There is no standard PRO instrument that is qualified 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 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 [attribute (e.g., *severity/frequency*)]
Daytime Symptoms	Patients treated with [*drugX*] reported significantly fewer days of asthma symptom [attribute (e.g., *severity/frequency*)]
Nighttime Symptoms	Patients treated with [*drugX*] reported significantly fewer nights of asthma symptom [attribute (e.g., *severity/frequency*)]
Individual Symptoms	[*drugX*] reduces [attribute of asthma symptom (e.g., severity/frequency of wheeze)]

Milestones

Milestone	Expected Date	Completed Date
Scoping Stage	03/02/2010	11/17/2010
Content Validity Stage		
Vendor selection and contracting	06/16/2011	02/28/2012
Completion of background research (literature review and 1st expert panel)	7/15/2012	
Completion of initial qualitative research and generate items (concept elicitation, selection and item generation – patients interviews & expert panels)	11/15/2012	
Refining initial instrument (cognitive interviewing, final expert panel, identification of ePRO platform, translatability assessment)	6/15/2013	
Qualitative research briefing package/document submitted to FDA for interim review	9/30/2013	
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

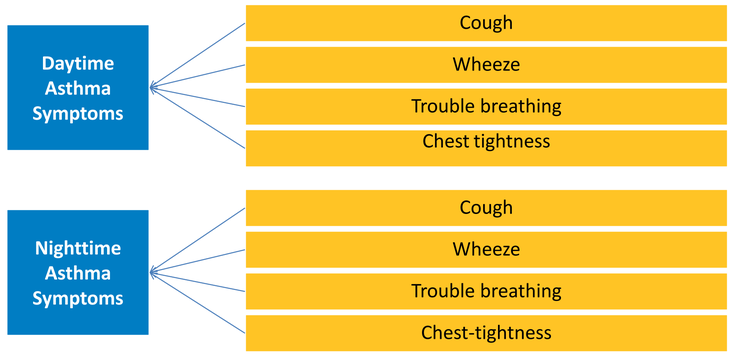
Endpoint Model for Treatment of Asthma

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

Target Population

- Adolescents and adults aged 12 years and older, with a clinical diagnosis of asthma with lung function impairment but without fixed airway obstruction
- Patients will be categorized in the guideline-defined levels of disease severity, which include mild through severe persistent asthma (GINA, 2009)

Hypothesized Conceptual Framework



Updates

- WG reviewed seven proposals and selected Adelphi Values for the qualitative research component of the Content Validity Stage (March 2011)
- The Asthma WG Co-chairs, C-Path representatives, and representatives of the NHLBI Task Force for Asthma Endpoints discussed the potential for collaboration/communication between the Asthma WG and the NHLBI Task Force (October 2011)
- Eleven sponsors have made a financial commitment to support the Content Validity Stage
- The project kickoff meeting was held with Adelphi Values (February 2012)
- Key opinion leaders (KOLs) have been identified and invited for the Expert Panel

Working Group Plans

Dissemination Plan

- Literature Review: American Thoracic Society (ATS) International Conference (May 2013) and International Society for Quality of Life Research (ISOQOL) Annual Meeting (October 2013)

Topics for Discussion

Concern Worth Noting

- WG has had no face-to-face contact with FDA review division regarding the planned Asthma Symptom Diary. All interaction has been through written communication. The WG feels that due to this limited and insufficient interaction, some issues pertaining to the focus and breadth of the Asthma Symptom Diary remain unaddressed

Unique Issues for the Working Group and the Resolutions

- There was a substantial delay in obtaining signed Project Agreements between C-Path and the 11 sponsoring firms
  - After eight months, all 11 Project Agreements were executed; C-Path has modified the process with the sponsors to expedite Project Agreement execution.
- Three PRO Consortium members indicated a willingness to contribute existing qualitative data for this project; however, all three may not contribute data.
  - The WG will proceed with the single data set contributed thus far

Lessons Learned

- Coordinating Committee has been exploring ways to streamline the Project Agreement process
- Consensus review by the WG of the seven submitted proposals was remarkably efficient

Working Group Participants

Company/Organization	Name
Actelion Pharmaceuticals, Ltd.	Elke Hunsche
Amgen Inc.	Brian Ortmeier, Gary Globe
AstraZeneca AB	Niklas Karlsson
Boehringer Ingelheim Pharmaceuticals, Inc.	Michael Engel, Dirk Esser
Forest Research Institute, Inc.	Michelle Mocarski, Paul Rowe
GlaxosmithKline LLC	Margaret Tabberer, Richard H. Stanford (co-chair)
Ironwood Pharmaceuticals, Inc.	Mollie Baird, Jeff Johnston
Janssen Global Services, LLC	Fang Chiou, Sarah Zander
Merck Sharp & Dohme Corp.	Linda Nelsen (co-chair)
Novartis Pharma AG	Jie Zhang, Karoly Kulich
Genentech, Inc.	Alison Greene

Contract Research Organization	Research Team
Adelphi Values	Adam Gater, Nicola Bonner, Linda Abetz, Chris Marshall, Kerry Turner, Rebecca Hall