Non-Small Cell Lung Cancer Working Group

Presented at the Sixth Annual PRO Consortium Workshop – Silver Spring, MD – April 29-30, 2015

PRO CONSORTIUM CRITICAL PATH INSTITUTE

Background

Rationale for Non-Small Cell Lung Cancer (NSCLC) Working Group (WG)

- PRO Consortium member firms and FDA advisors identified NSCLC as a priority area
- As current therapies for advanced NSCLC are not curative, any new therapy should demonstrate control of distressing disease symptoms; including this in the label would enable a standard method for patients and providers to compare benefit between treatments
- While valid, reliable, and responsive PRO instruments exist for the assessment of NSCLC symptoms, none meet the current standards for an FDA-approved label claim
- FDA had stated a 'fit for purpose' measure to assess NSCLC symptoms would be helpful in evaluating the patient benefit of new therapies

Goal of the NSCLC WG

- To develop a PRO measure for patient-experienced symptoms in advanced NSCLC (Stage IIIB/IV) and Eastern Cooperative Oncology Group (ECOG) performance status of 0-2 for use in clinical trials as a secondary endpoint to establish treatment benefit

Targeted Labeling Language

- Patients treated with [Product X] reported an improvement in the core symptoms of NSCLC or a delay in the deterioration of the core symptoms of NSCLC
  - Improvement for patients who are symptomatic at baseline
  - Delayed deterioration for patients who are asymptomatic at baseline

Milestones

Milestone	Expected Date	Completed Date
Content Validity Stage		
Vendor selection and contracting	April 2012	September 2012
Completion of background research (literature review and 1st expert panel)	December 2012	February 2013
Submit Concept Elicitation Protocol to FDA for consultation and advice	November 2013	October 2013
Draft Instrument: Complete initial qualitative research and generate items (concept elicitation interviews, item generation, expert panel input, and initial round of cognitive interviews)	4Q2013	December 2013
Submit Qualitative Research Summary Briefing Document and protocol for quantitative study to FDA for review and feedback	2Q2014	June 2014
Submit updates to FDA for review and feedback (rounds 2-3 cognitive interviews, final cognitive interview report, expert panel meeting, and updated instrument)	3Q2014	April 2015
Conduct quantitative pilot study	3Q2015	
Complete documentation of content validity and cross-sectional evaluation of other measurement properties	4Q2015	
Submit exploratory endpoint qualification briefing document to FDA	1Q2016	

Content of Interest

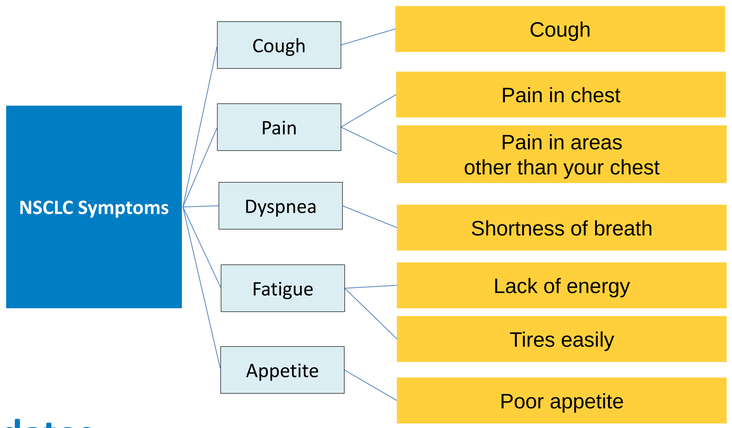
Endpoint Model for Treatment of NSCLC

Endpoint Hierarchy	Endpoint Concept(s)	Endpoint Type
Primary	▪ Progression-Free Survival (PFS) - Response Evaluation Criteria in Solid Tumors (RECIST) ▪ Overall Survival	Biomarker Survival
Secondary	▪ Improvement in NSCLC Symptoms – NSCLC symptom inventory ▪ Delay in time to deterioration of NSCLC symptoms ▪ Delay in time to onset of symptoms of NSCLC	PRO

Target Population

- Patients 18 years and older
- Advanced NSCLC (Stage IIIB/IV) with ECOG performance status of 0-2, regardless of line of therapy

Hypothesized Conceptual Framework



Updates

- Instrument development updates:
  - Decided on instrument name: *Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ)*
  - YPrime selected as ePRO system provider
  - Electronic version evaluated in Wave 2 and Wave 3 cognitive interviews
  - FDA comments received December 2014 with general agreement on approach for quantitative pilot study
  - Wave 3 cognitive interviews completed in March 2015
  - NSCLC-SAQ uses 7-day recall and 5-point verbal rating scale

- NSCLC-SAQ to be used in quantitative pilot study will also be used in LungMAP
  - Biomarker driven interventional study of patients with squamous NSCLC
  - Sponsors include the National Cancer Institute, the Southwest Oncology Group (SWOG), pharmaceutical companies, and advocacy groups

Working Group Plans

Next Steps

- Submit results of Wave 2 and 3 cognitive interviews to the FDA in response to December 2014 comments
- Launch quantitative pilot study – target April 2015

Information Dissemination Plan

- Abstract accepted for publication only at American Society of Clinical Oncology (ASCO) 2014 annual meeting
- Recent abstracts submitted to:
  - 16th World Conference on Lung Cancer to be held in Denver, CO; September 6 - 9, 2015
  - ISOQOL 22nd Annual Conference to be held October 21 - 24, 2015 in Vancouver, Canada

Topics for Discussion

Working Group interaction with the FDA

- FDA recommended ensuring recruitment of subjects with Stage IV NSCLC, with performance status 2, and treatment-naïve
  - Protocol and statistical analysis plan were updated to ensure adequate recruitment
- FDA suggested assessing symptom intensity at its worst for pain
  - Recommended change was tested during Wave 3 of cognitive interviews and based on interview results, the pain items were revised to reflect "worst" pain
- FDA expressed concern about definition of "usual activities" for dyspnea
  - Wave 3 cognitive interviews documented subject description of "usual activities" and item was updated to include "usual activities" in the stem

Challenges:

- How to address scoring of symptoms (i.e., pain and fatigue) assessed by two items

Working Group Participants

Company/Organization	Name
AbbVie	Saurabh Ray
Boehringer Ingelheim	Louis Denis, Dagmar Kaschinski, Juliane Lungershausen
Bristol-Myers Squibb	John Penrod, Lucinda Orsini , Sarah Lewis
Eli Lilly and Company	April Naegeli, Astra Liepa (Co-Chair)
Genentech, Inc.	Alicyn Campbell (Co-Chair), Kendra DeBusk, Liz Piault-Louis
Merck Sharp & Dohme Corp.	Jean Marie Arduino, Anne Deitz, Smita Kothari
Novartis Pharmaceuticals	Vasudha Bal
Expert Panel Members	**Affiliation**
Richard Gralla, MD	Albert Einstein College of Medicine
Suresh Ramilingham, MD	Emory University
David Cella, PhD	Northwestern University
Donald Patrick, PhD	University of Washington
Ethan Basch, MD	University of North Carolina at Chapel Hill
Shirish Gadgeel, MD	Karmanos Cancer Center
Contract Research Organization	**Name**
Health Research Associates (HRA)	Don Bushnell, Mona Martin, Kelly McCarrier, Michael Scanlon, Thomas Atkinson (MSKCC)