Non-Small Cell Lung Cancer Working Group

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	Apr 2012	Sep 2012
Completion of background research (literature review and 1st expert panel)	Dec 2012	Feb 2013
Submit Concept Elicitation Protocol to FDA for consultation and advice	Nov 2013	Oct 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	Dec 2013
Submit Qualitative Research Summary Briefing Document and protocol for quantitative study to FDA for review and feedback	2Q2014	Jun 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	Apr 2015
Discussion with FDA for review and feedback (updated instrument) prior to launch of quantitative pilot study	3Q2014	Jun 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	

PRO Instrument Highlights

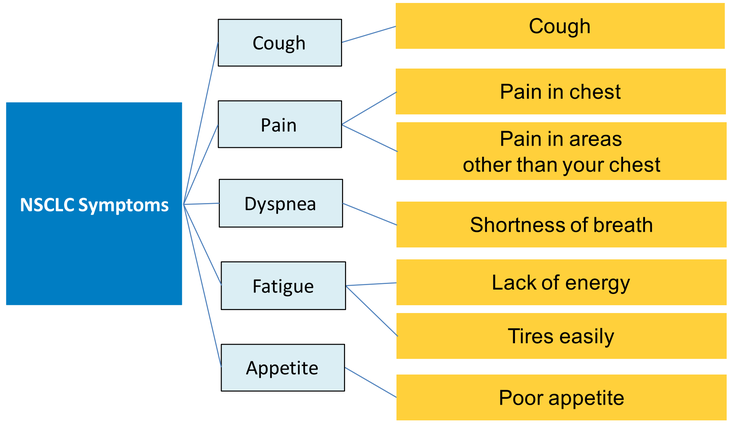
Endpoint Model for Treatment of NSCLC

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



Draft Instrument - *Non-Small Cell Lung Cancer Symptom Assessment Questionnaire* (*NSCLC-SAQ*)

- *NSCLC-SAQ* has seven items addressing five symptom domains
- *NSCLC-SAQ* uses a 7-day recall period and a 5-point verbal rating scale
- YPrime selected as ePRO system provider
- Initial electronic data collection mode for the pilot quantitative pilot study will be a tablet computer
- *NSCLC-SAQ* to be used as an exploratory endpoint in LungMAP
  - A biomarker driven interventional study of patients with squamous NSCLC
  - Sponsors include the National Cancer Institute, Southwest Oncology Group (SWOG), pharmaceutical companies, and advocacy groups

Working Group Plans

Information Dissemination Plan

- Presentations to be given at the International Society for Quality of Life Research (ISOQOL) 22nd Annual Conference to be held October 21-24, 2015, in Vancouver, BC
  - McCarrier K, et al. "Identification of Patient-Relevant Non-Small Cell Lung Cancer (NSCLC) Symptoms through Semi-Structured Qualitative Interviews"
  - Scanlon M, et al. "Incorporating the Patient's Voice into Instrument Development: How do Patients Describe the Impact of Non-small Cell Lung Cancer on Their Breathing?"
  - Atkinson T, et al. "Use of Concept Elicitation Interviews to Determine Potential Differences in Disease-related Symptom Concepts Between Early- Versus Advanced-stage Non-small Cell Lung Cancer (NSCLC) Patients"
- Presentation to be given at the 16th World Conference on Lung Cancer (WCLC) to be held September 6-9, 2015, in Denver, CO
  - Campbell A, et al. "Assessing Patient-Reported Symptoms in Non-Small-Cell Lung Cancer Clinical Trials"

Quantitative Pilot Study

- FDA comments received December 2014 with general agreement on approach for quantitative pilot study
- Quantitative pilot study underway (n=150) with data collected via touchscreen tablet at study sites (i.e., oncology clinics)

FDA Submission

- Plan to submit exploratory endpoint qualification dossier to FDA in first quarter of 2016

Next Steps

- Identify clinical trial(s) in which to incorporate the *NSCLC-SAQ* as an exploratory endpoint

Working Group Participants

Company/Organization	Representatives
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, Kendra DeBusk (Co-Chair), Liz Piault-Louis
Janssen Global Services	Renee Pierson
Merck Sharp & Dohme Corp.	Jean Marie Arduino, Anne Deitz, Smita Kothari
Novartis Pharmaceuticals	Denise D'Alessio
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	**Research Team**
Health Research Associates (HRA)	Don Bushnell, Mona Martin, Kelly McCarrier, Michael Scanlon, Thomas Atkinson (MSKCC)
ePRO System Provider	**Representative**
YPrime	Jennifer Crager