Non-Small Cell Lung Cancer Working Group

Presented at the Ninth Annual PRO Consortium Workshop – Silver Spring, MD – April 25-26, 2018

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 product label would enable a standard method for patients and providers to compare benefit among treatments
- While reliable and responsive PRO instruments exist for the assessment of NSCLC symptoms, none appeared to 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 treatment benefit of new therapies

Goal of the NSCLC WG

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

Targeted Labeling Language

- Patients treated with [*Drug 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 symptomatic or asymptomatic at baseline

Milestones

Milestone	Completed Date
Vendor selection and contracting	SEP 2012
Completion of background research (literature review and 1st expert panel)	FEB 2013
Submit Concept Elicitation Protocol to FDA for consultation and advice	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)	DEC 2013
Submit Qualitative Research Summary Briefing Document and protocol for quantitative study to FDA for review and feedback	JUN 2014
Submit updates to FDA for review and feedback (rounds 2 and 3 cognitive interviews, final cognitive interview report, expert panel meeting, and updated instrument)	APR 2015
Discussion with FDA for review and feedback (updated instrument) prior to launch of quantitative pilot study	JUN 2015
Complete quantitative pilot study	JUL 2016
Complete documentation of content validity and cross-sectional evaluation of other measurement properties	OCT 2016
Submit Qualification Briefing Package to FDA for exploratory use of *NSCLC-SAQ*	MAR 2017
Qualification statement issued for use of *NSCLC-SAQ* in exploratory studies	MAR 2018

Highlights

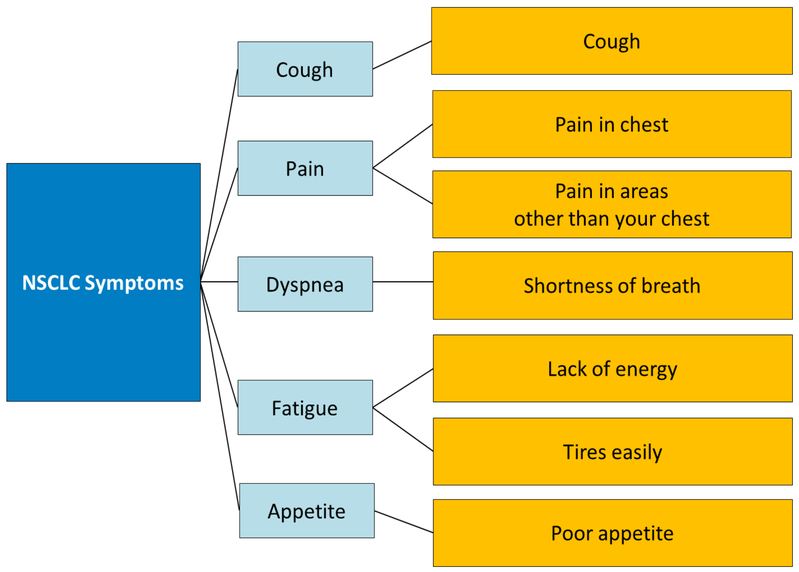
Example Endpoint Model for Treatment of NSCLC

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-SAQ* Or ▪ Delay in time to deterioration of NSCLC symptoms – *NSCLC-SAQ*	PRO

Target Population

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

Conceptual Framework



Measure – *Non-Small Cell Lung Cancer Symptom Assessment Questionnaire* (*NSCLC-SAQ*)

Core Items: Seven items addressing five symptom domains
Recall Period: 7-day
Response Options: 5-level verbal rating scale
Symptom Attributes: Intensity or frequency as a measure of severity
Data Collection Mode: Tablet computer used for the quantitative pilot study

Working Group Updates

Completed Activities

- At FDA request, Quantitative Pilot Study Report and quantitative data submitted to FDA as part of Qualification Briefing Package instead of as separate submission
- Responses to FDA's Information Requests submitted in September and October 2017
- Received qualification of *NSCLC-SAQ* in March 2018

Information Dissemination

- McCarrier et al. (2016) Qualitative development and content validity of the *Non-small Cell Lung Cancer Symptom Assessment Questionnaire* (*NSCLC-SAQ*), a patient-reported outcome instrument. *Clinical Therapeutics* 38(4):794-810.
- Poster titled 'Evaluating the *Non-Small Cell Lung Cancer Symptom Assessment Questionnaire* (*NSCLC-SAQ*): Results from the Quantitative Pilot Study presented at the 17th World Congress on Lung Cancer, December 4-7, 2016 in Vienna, Austria
- A manuscript on quantitative evaluation of the *NSCLC-SAQ* will be written and submitted for publication following its qualification for exploratory use

COA Qualification from FDA

- The qualification of the *NSCLC-SAQ* represents a major milestone for the PRO Consortium and specifically for the NSCLC WG
- Drug developers are encouraged to discuss with FDA inclusion of this novel instrument in their lung cancer drug development programs
- Further evaluation of the instrument's longitudinal properties and the interpretation of clinically meaningful within-patient change in score using clinical trial data is needed

Working Group Participants

Company/Organization	Representatives
AbbVie	Katy Benjamin, PhD
AstraZeneca	Anna Ryden, PhD
Boehringer Ingelheim	Dagmar Kaschinski, MBA; Juliane Lungershausen, MSc; Claudia Hastedt, Dr. phil.
Bristol-Myers Squibb	John Penrod, PhD, MS; James W. Shaw, PharmD, PhD
Eli Lilly and Company	Astra Liepa, PharmD (Co-Chair); Jonathan Gable
EMD Serono	Vivek Pawar, PhD; Ronaldo Fujii, PhD
Genentech	Thomas Karagiannis, PharmD, MS (Co-Chair); Alicyn Campbell
Janssen Global Services	Renee Pierson, MBA
Merck Sharp & Dohme	Josephine Norquist, MS; Tom Burke, PharmD, PhD
Novartis Pharmaceuticals	Denise D'Alessio, MBA
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, MA; Mona Martin, RN, MPA; Kelly McCarrier, PhD, MPH; Larissa Stassek, MPH; Thomas Atkinson, PhD (MSKCC)
ePRO System Provider	**Representative**
YPrime	Michael Hughes