Non-Small Cell Lung Cancer (NSCLC) Working Group

Presented at the Fifth Annual PRO Consortium Workshop – Silver Spring, MD – April 29-30, 2014

PRO CONSORTIUM
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Background

Rationale for 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' method 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 (stages III/IV and ECOG performance status of 0-2) for use in clinical trials as a primary or 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
Scoping Stage		July 27, 2011
Content Validity Stage		
Vendor selection and contracting	April 2012	Vendor selected January 2012; Project kickoff 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	
Submit updates to FDA for review and feedback (rounds 2-3 cognitive interviews, final cognitive interview report, expert panel meeting, and updated instrument)	3Q2014	
Complete documentation of content validity and cross-sectional evaluation of other measurement properties	2Q2015	
Submit briefing document to FDA for qualification of the symptom inventory for use in exploratory studies	4Q2015	

Content of Interest

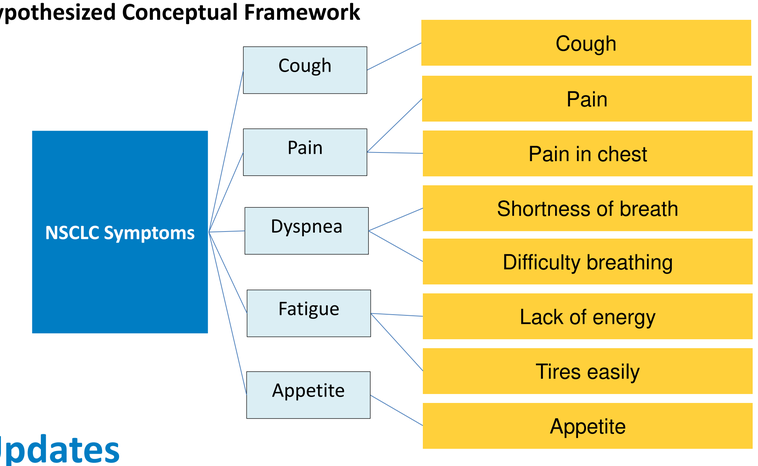
Endpoint Model for Treatment of NSCLC

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 III/IV) with Eastern Cooperative Oncology Group (ECOG) performance status of 0-2, regardless of line of therapy
- We will also be assessing symptom experience of early stage (I/II) patients to determine the applicability of the instrument to all stages of disease, and for patients whose symptoms worsen

Hypothesized Conceptual Framework



Updates

- Concept Elicitation/Item Generation: The most commonly expressed symptom was fatigue. Other symptoms included general pain, chest pain, cough, shortness of breath, difficulty breathing, appetite change, and coughing up blood (hemoptysis). Items were drafted to assess either frequency or severity for nine distinct symptoms using a 7-day recall period.
- Wave 1 cognitive interviews were conducted using VRS and NRS response scale versions of the initial draft instrument. Findings from the interviews, electronic implementation assessment, and translatability assessment resulted in moving forward with the VRS version of the instrument named the NSCLC Symptom Assessment Questionnaire (NSCLC-SAQ).
- Additional oncologists were invited to join the expert panel in January 2014 and were included in the review of the cognitive interview results in February 2014.
- The hemoptysis item was removed and the remaining items in the VRS version of the instrument have been updated per all reviews .
- The cognitive interview guide to be updated to include probing in Wave 2 and 3 for possible item reduction for the dyspnea, pain, and fatigue domains .

Working Group Plans

Next Steps

- Submit the results of the qualitative research through Wave 1 of cognitive interviews, the updated instrument, and the quantitative study design to the FDA
- Select an ePRO system provider and implement the NSCLC-SAQ on a tablet computer for Wave 2 and 3 of cognitive interviews
- Update budget for quantitative pilot study and initiate project amendments
- Conduct Wave 2 and 3 cognitive interviews, and submit results to the FDA

Dissemination plan

- Abstract accepted for publication at ASCO 2014

Topics for Discussion

Concerns Worth Noting

- QRT requested that subjects with a wider range of performance status (ECOG 3 and 4)be included in the qualitative research
- QRT suggested WG has multiple contexts of use – WG intends a single, narrow COU

Issues for the Working Group and the Resolutions

- Mitigate the impact of treatment side effects from confounding concept elicitation
  - Treatment side effects must be resolved or only at Grade 1 before interview
- Recruitment of early stage NSCLC patients prior to potentially curative interventions (e.g., surgery)
  - Use of sites that are involved with initial diagnosis of NSCLC
- Requirement to understand the clinical course of the disease and its interactions with treatment-induced side effects when designing the inclusion / exclusion criteria
  - Inclusion of thoracic oncologists in the expert panel

Challenges:

- Recruitment of subjects to meet demographic distribution, as well as distribution of NSCLC stage with/without COPD
- Length of time to have original sponsor agreements executed, and upcoming amendments for the quantitative pilot study

Working Group Participants

Company/Organization	Name
AbbVie	Saurabh Ray
Boehringer Ingelheim Pharmaceuticals, Inc.	Louis Denis, Dagmar Kaschinksi, Juliane Lungershausen
Bristol-Myers Squibb	John Penrod, Lucinda Orsini , Sarah Lewis
Eli Lilly and Company	Nicki Bush, Astra Liepa (Co-Chair)
Genentech, Inc.	Jessica Burton, Alicyn Campbell (Co-Chair), Kendra DeBusk, Liz Piault-Louis
Merck Sharp & Dohme Corp.	Jean Marie Arduino, Anne Deitz, Smita Kothari, Jay Pearson
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)