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 appear to meet the current standards for an FDA-approved label claim

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 support treatment benefit

Targeted Labeling Language
- Patients treated with (Product X) reported an improvement in the core symptoms of NSCLC
- Improvement for patients who are symptomatic at baseline
- Delayed deterioration for patients who are asymptomatic at baseline

Milestones

<table>
<thead>
<tr>
<th>Milestone</th>
<th>Expected Date</th>
<th>Completed Date</th>
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<tbody>
<tr>
<td>Background</td>
<td>Apr 2012</td>
<td>Sep 2012</td>
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<tr>
<td>Completion of background research (literature review and 1st expert panel)</td>
<td>Dec 2012</td>
<td>Feb 2013</td>
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<tr>
<td>Draft instrument - Complete initial qualitative research and generate items (concept elicitation interviews, item generation, expert panel input, and initial round of cognitive interviews)</td>
<td>Nov 2013</td>
<td>Oct 2013</td>
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<tr>
<td>Draft instrument - submit protocol to FDA for consultation and advice</td>
<td>Nov 2013</td>
<td>Oct 2013</td>
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<tr>
<td>Draft instrument - submit protocol for quantitative study to FDA for review and feedback</td>
<td>Nov 2013</td>
<td>Oct 2013</td>
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<tr>
<td>Draft instrument - submit updates to FDA for review and feedback (rounds 2-3 cognitive interviews, final interview report, expert panel meeting, and updated instrument)</td>
<td>Dec 2013</td>
<td>Jan 2014</td>
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<tr>
<td>Conduct qualitative interview study</td>
<td>Apr 2015</td>
<td>Apr 2015</td>
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<tr>
<td>Conduct qualitative interview study</td>
<td>Mar 2016</td>
<td>Mar 2016</td>
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<tr>
<td>Complete documentation of content validity and cross-sectional evaluation of other measurement properties</td>
<td>Apr 2016</td>
<td>Apr 2016</td>
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<tr>
<td>Submit exploratory endpoint qualification dossier to FDA</td>
<td>Apr 2016</td>
<td>Apr 2016</td>
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Non-Small Cell Lung Cancer Working Group
Presented at the Seventh Annual PRO Consortium Workshop – Silver Spring, MD – April 27-28, 2016

Highlights

Example Endpoint Model for Treatment of NSCLC

<table>
<thead>
<tr>
<th>Endpoint Hierarchy</th>
<th>Endpoint Concept(s)</th>
<th>Endpoint Type</th>
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<tbody>
<tr>
<td>Primary</td>
<td>Progression-Free Survival (PFS) - Response Evaluation Criteria in Solid Tumors (RECIST)</td>
<td>Biomarker Survival</td>
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<tr>
<td>Overall Survival</td>
<td></td>
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<tr>
<td>Secondary</td>
<td>Improvement in NSCLC symptoms – NSCLC-SAQ</td>
<td>PRO</td>
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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-level verbal rating scale
- Electronic data collection mode for quantitative pilot study is a tablet device
- NSCLC-SAQ is being 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
- Boehringer Ingelheim will be using the NSCLC-SAQ in 2 global Phase 3 clinical trials - Q3 2016

Working Group Plans

Information Dissemination Plan
- Presentations given at the International Society for Quality of Life Research (ISQLQ) 22nd Annual Conference held October 21-24, 2015, in Vancouver, BC
- McCarry KP, et al. "Identification of Patient-Relevant Non-Small Cell Lung Cancer (NSCLC) Symptoms through Semi-Structured Qualitative Interviews"
- Atkinson TM, 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 given at the 16th World Conference on Lung Cancer (WCLC) held September 6-9, 2015, in Denver, CO — Campbell A, et al. "Assessing Patient-Reported Symptoms in Non-Small-Cell Lung Cancer Clinical Trials"
- Abstract on quantitative data to be submitted to 17th WCLC to be held December 4-7, 2016 in Vienna, Austria

Quantitative Pilot Study and Next Steps
- FDA comments received December 2014 with general agreement on approach for quantitative pilot study; study currently underway (N=150) with NSCLC-SAQ data collected at study sites (i.e., oncology clinics) via a tablet computer
- The pilot study data will be analyzed and evidence generated to support submission of a briefing package to FDA for qualification of the NSCLC-SAQ for use in exploratory studies

Working Group Participants

Company/Organization | Representatives
---|---
AbbVie | Patrick Bonnet, PharmD, MS
Boehringer Ingelheim | Dagmar Kaschinski; Juliane Lengershausen, MSc; Claudia Hastedt
Bristol-Myers Squibb | John Penrod, PhD, MS; LuCinda Orsini, DFM; Sarah Lewis, MPSH
Eli Lilly and Company | Astra Liepa, PharmD (Co-Chair); David Ayer, PhD
Genentech, Inc. | Kendra Delbrouck, PhD (Co-Chair); Allison Campbell, MPH; Thomas Karagianis, PharmD, MS
Janssen Global Services | Renee Pierson, MBA; Chuan-Fang Chiou, PhD
Merck Sharp & Dohme | Jean Marie Arduino, ScD; Josephine Norquist, MS; Tom Bunkle, PharmD, PhD
Novartis Pharmaceuticals | Denise D’Alessio, MBA
YPrime | Michael Hughes; Cindy Howry, MS

Expert Panel Members

Affiliation
- Richard Gralla, MD | Albert Einstein College of Medicine
- Suresh Ramilingham, MD | Emory University
- Ethan Basch, MD | University of North Carolina at Chapel Hill
- Donald Patrick, PhD | Northwestern University
- Donald Patrick, PhD | University of North Carolina at Chapel Hill
- Shrish Gadgeel, MD | Karmanos Cancer Center
- John Penrod, PhD | Northwest University
- Jonathan Strosberg, MD | Emory University
- David Colla, PhD | Janssen Global Services
- David Colla, PhD | Janssen Global Services
- Michael Hughes | Novartis Pharmaceuticals
- Cindy Howry, MS | YPrime

Health Research Associates

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  Larissa Stassek, Tom Atkinson, PhD (MSKCC)
- ePRO System Provider
  - Representative
  - Michael Hughes; Cindy Howry, MS

YPrime
- Representative
  - Michael Hughes; Cindy Howry, MS