Small Cell Lung Cancer Working Group

Prepared for the 11th Annual PRO Consortium Workshop (April 22-23, 2020), which was cancelled due to COVID-19

PRO CONSORTIUM CRITICAL PATH INSTITUTE

Background

Rationale for Small Cell Lung Cancer (SCLC) Working Group

- PRO Consortium member firms and FDA advisors identified SCLC as a priority area for the qualification of a PRO measure focused on disease symptoms to evaluate the clinical benefit of new therapies.
- As current therapies for limited and extensive stage SCLC are not curative, any new therapy should demonstrate meaningful relief from distressing disease-related symptoms; including standardized symptom outcome information in the product label would enable patients and providers to compare benefit among treatments.
- While reliable and responsive PRO measures exist for the assessment of lung cancer symptoms, none were developed specifically for SCLC or believed to have met the current regulatory expectations for supporting an FDA-approved label claim.
- With FDA qualification of the *Non-Small Cell Lung Cancer Symptom Assessment Questionnaire* (*NSCLC-SAQ*) in April 2018, the SCLC Working Group was convened to work toward FDA qualification of a patient-reported measure of SCLC symptom severity for use in assessing clinical benefit in SCLC treatment trials.

Goal of the SCLC Working Group

- To derive a concise PRO measure to assess the severity of patient-experienced symptoms in limited and extensive stage SCLC for use in clinical trials to support clinical benefit

Targeted Labeling Language

- Patients treated with [*Drug X*] reported a decrease in core SCLC symptom severity or a delay in the deterioration of the core SCLC symptoms.
  - Decrease in symptom severity for patients who are symptomatic at baseline
  - Delayed symptom deterioration or symptom onset for patients who are symptomatic or asymptomatic at baseline

Milestones

Milestone	Expected Date	Completed Date
Letter of Intent submission for proposed SCLC symptom measure to FDA		MAR 2020
Receipt of reviewability determination letter from FDA		APR 2020
Acceptance of proposed SCLC symptom measure by FDA into the COA Qualification Program	Q3 2020	
Completion of qualitative interviews to assess content validity of the proposed SCLC symptom measure in the target population	TBD	
Qualification Plan submission to FDA	TBD	
Full Qualification Package submission to FDA	TBD	

Highlights

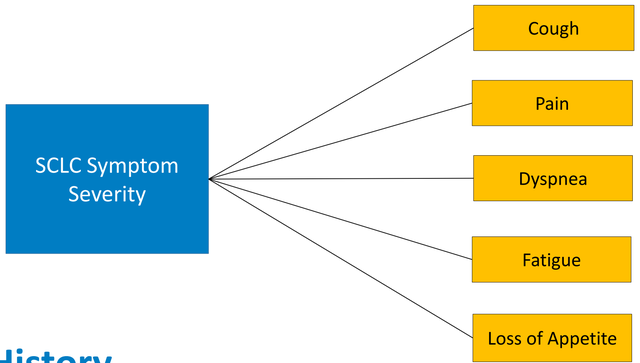
Example Endpoint Model for Treatment of SCLC

Endpoint Hierarchy	Endpoint Concept(s)	Endpoint Type
Primary	▪ Progression-Free Survival (PFS) - Response Evaluation Criteria in Solid Tumors (RECIST) ▪ Overall Survival ▪ Objective Response Rate (ORR)	Biomarker Survival
Secondary	▪ Decrease in symptom severity for patients who are symptomatic at baseline ▪ Delayed symptom deterioration or symptom onset for patients who are symptomatic or asymptomatic at baseline	PRO

Target Population

- Patients 18 years and older
- Clinician-confirmed diagnosis of limited or extensive stage SCLC with Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2, regardless of line of therapy being administered

Proposed Conceptual Framework



History

- The *Non-Small Cell Lung Cancer Symptom Assessment Questionnaire* (*NSCLC-SAQ*), qualified by FDA for a limited context of use in drug development for individuals with NSCLC, will serve as the basis for the proposed SCLC symptom measure.
- Modifications will be considered to optimize the measure for the new context of use.
- All five existing domains are anticipated to be retained, with the opportunity to explore any additional domains during upcoming qualitative interviews.
- Two sets of items (pain and fatigue), however, will be revisited to determine:
  - if a single overall pain item is more appropriate than the two separate pain items currently in the *NSCLC-SAQ* (pain in chest, pain in areas other than chest), and
  - whether one of the current fatigue items (low energy, tires easily) from the *NSCLC-SAQ* can be dropped due to redundancy as these items, although they both resonated with a high percentage of respondents (qualitatively), have been highly correlated (quantitatively) in previous research.
- These aspects will be evaluated in the proposed qualitative interviews (and may be further explored in a subsequent quantitative pilot study) with individuals diagnosed with SCLC.

Working Group Activities

Completed Activities

- Two firms supporting the SCLC Working Group have shared findings from their literature reviews and preliminary concept elicitation research conducted to identify SCLC symptoms for inclusion in a PRO measure, one focusing on participants with extensive stage disease and the other including both limited and extensive stage SCLC.
  - The findings demonstrated that, similar to NSCLC, the symptoms of cough, pain, shortness of breath, fatigue, and loss of appetite were identified as important to individuals with SCLC.
  - This evidence is supportive of moving forward with the *NSCLC-SAQ* as a starting point for the PRO measure for SCLC treatment trials.
- Letter of Intent was submitted to FDA in March 2020 and deemed reviewable in April.

Next Steps

- Await FDA response to the Letter of Intent regarding acceptance of the proposed SCLC symptom measure into the COA Qualification Program
- Release a request for proposal to conduct qualitative research to ensure content validity of the derived measure among individuals who have been diagnosed with SCLC and, subsequently, partner with the chosen vendor
- Engage an advisory panel of up to five clinicians, measurement experts, and patient representatives/advocates to be involved in the item refinement process
- Conduct qualitative interviews with participants with SCLC to determine whether the five concepts/domains included in the proposed conceptual framework reflect the appropriate content (i.e., concept confirmation) and to evaluate the proposed SCLC symptom measure for its appropriateness within the target population:
  - Confirm core symptom concepts through introductory concept elicitation exercise to evaluate relevance and comprehensiveness;
  - Evaluate the content validity and comprehensibility of the proposed SCLC symptom measure through detailed cognitive interview questions; and
  - Conduct preliminary exploration of clinically meaningful change with participants
- Refine the proposed SCLC symptom measure in an iterative manner throughout the qualitative research, as appropriate

Working Group Participants

Company/Organization	Representative
AstraZeneca AB	Emuella Flood
Boehringer Ingelheim	Maarten Voorhaar, MSc; Matt Sidovar, MSc, MA
Bristol-Myers Squibb	Steven Blum, MBA, MA (Co-Chair)
Eli Lilly and Company	Astra Liepa, PharmD; Jonathon Gable, MPA; Nicki Bush, MHS
Genentech/Roche	Tom Willgoss, PhD; Megan Chen, MPH
GlaxoSmithKline, LLC	Laurie Eliason, MPH; Linda Nelsen, MHS
Janssen Global Services, LLC	Renee Pierson, MBA; Carol Jamieson, BSc
Merck Sharp & Dohme Corporation	Josephine Norquist, MS; Paivi Miskala, PhD
Novartis Pharmaceuticals	Sue Vallow, RPh, MBA, MA (Co-Chair); Denise D'Alessio, MBA; Stefanie Knoll, PhD