Small Cell Lung Cancer Working Group

12th Annual PRO Consortium Workshop – Held Virtually on April 14-15, 2021

PRO CONSORTIUM
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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 assessment of 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
Acceptance of proposed SCLC symptom measure by FDA into the COA Qualification Program		JUL 2020
Completion of qualitative interviews to assess content validity of the proposed SCLC symptom measure in the target population	Q4 2021	
Qualification Plan submission to FDA	TBD	
Full Qualification Package submission to FDA	TBD	

Highlights

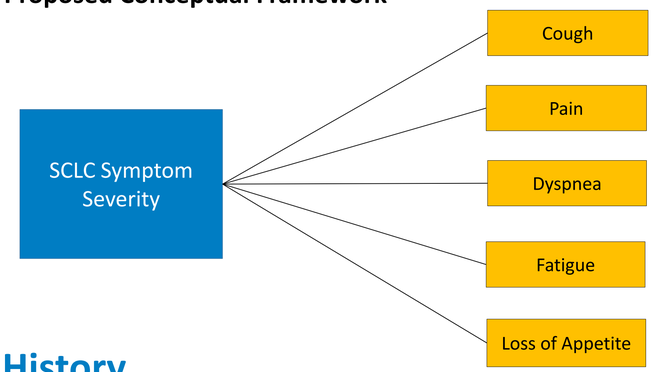
Example Endpoint Model for Treatment of SCLC

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 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 PRO

Target Population

- Persons 18 years of age and older with a clinician-confirmed diagnosis of limited or extensive stage SCLC and 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*), which was qualified by FDA for use in drug development for 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 5 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 2 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 planned 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 shared findings from their literature reviews and preliminary concept elicitation research conducted to identify SCLC symptoms for inclusion in a PRO measure in the target population.
  - Findings demonstrated that, similar to NSCLC, symptoms of cough, pain, shortness of breath, fatigue, and loss of appetite were 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.
- FDA accepted the proposed SCLC symptom measure into the COA Qualification Program in July 2020.
- Review of more recent literature was conducted to confirm the key concepts for inclusion in a SCLC symptom measure.
- Pharmerit was selected as the vendor to conduct qualitative study to confirm content validity of the derived measure among individuals diagnosed with limited and extensive stage SCLC.

Next Steps

- Engage an Advisory Panel of approximately 6 clinicians and patient advocates to be involved in the study design and item refinement process
- Complete qualitative interviews with participants (n=30) with SCLC to determine whether the 5 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
- Once SCLC symptom measure is refined, prepare and submit Qualification Plan to FDA

Working Group Participants

Company/Organization	Representative
Amgen	Martin Paczkowski, MPH
AstraZeneca AB	Nenad Medic, PhD
Boehringer Ingelheim	Maarten Voorhaar, MSc; Matt Sidovar, MSc, MA
Bristol Myers Squibb	Steven Blum, MBA, MA (Co-Chair)
Eli Lilly and Company	Elizabeth Nicole Bush, MHS; Lee Bowman, PhD
Genentech/Roche	Dylan Trundell, MSc; Megan Chen, MPH
GlaxoSmithKline, LLC	Linda Nelsen, MHS; Jennifer Hanlon, MPH; Laurie Eliason, MPH
Janssen Global Services, LLC	Renee Pierson, MBA; Carol Jamieson, BSc; Kevin Liu, PharmD
Jazz Pharmaceuticals	Susan Morris, PhD; Dylan Supina, PhD; Bhavini Srivastava, MS
Merck Sharp & Dohme Corp	Josephine Norquist, MS; Paivi Miskala, MSPH, PhD
Novartis Pharmaceuticals	Sue Vallow, RPh, MBA, MA (Co-Chair); Denise D'Alessio, MBA; Stefanie Knoll, PhD
Research Partners	Research Team
Pharmerit/OPEN Health	Kelly McCarrier, MPH, PhD; Laura DiGiovanni, MA; Rachel Shah, BS; Emily Evans, MSc
Vector Psychometric Group	R. J. Wirth, PhD; Carrie Houts, PhD; Tracy Nishida, PhD