Shedding Light on Patient-Reported Outcome Measure Utilization across NSCLC Therapies

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BACKGROUND

- Patient reported outcome (PRO) measures are integral to oncology, capturing patient's perception, and complementing surrogate endpoints in evaluating treatment benefits[1,2]
- In non small cell lung cancer (NSCLC), where both disease and treatments can affect daily living and quality of life (QOL), PROs are increasingly important in measuring treatment impact, benefit-risk assessment, and supporting patient-care[3]
- As oncology care continues to shifts towards patient-centered approaches, PROs are recommended in NSCLC clinical trials, although their application remains inconsistent
- Characterizing the use of PRO in NSCLC trials may help assess their role in improving patient care, informing, regulatory decisions, and shaping future research

OBJECTIVES

This study characterized the use of PRO measures in United States (US)-based NSCLC monotherapy trials by assessing:

- PRO measures usage (defined as inclusion in trials) over time (2015-2026)
- PRO measures usage across drug classes
- PRO concept coverage (domains, subdomains, and items) across NSCLC disease characteristics and treatment emergent adverse events (TEAE) by drug classes

METHODS

Figure 1: Study Methodology

A — Data Source

- **Trial Information**: CT.Gov Database[4]
- **PRO Measures**: eProvide Database[5]

B — Trial Identification Criteria

- **Mesh Term:** Carcinoma, Non-Small Cell Lung Cancer
- **Start date:** >01/01/2015
- **Sponsor Agency Class:** Industry
- **Study Type:** Interventional
- **Study Phase:** 1/2/3
- **Country:** United States
- **Study Status:** Completed & Ongoing

C — Eligible Trials (n = 862)

NSCLC trials based on the trial criteria were identified

D — Trials with PRO Measures (n = 138)

Trials with relevant PRO measures were identified

E — PRO-Inclusive Monotherapy Trials (n = 67)

Monotherapy trial arms were identified

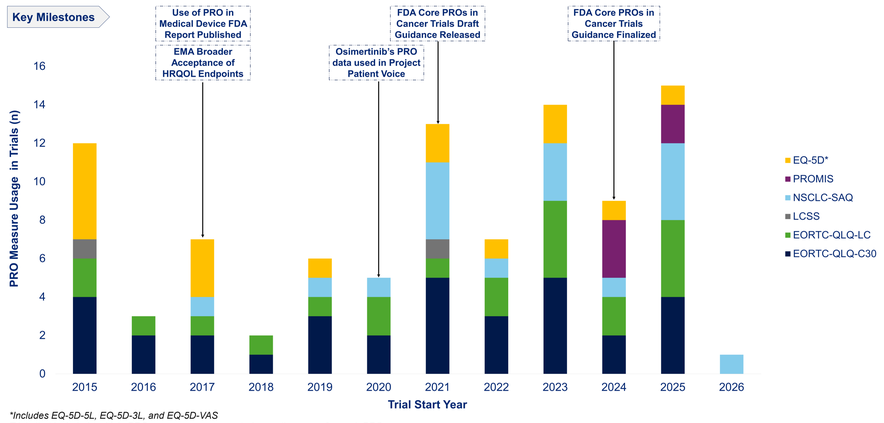
F — PRO-Inclusive Monotherapy Trials with Reported Data (n = 13)

Monotherapy trial arms with data were identified

- Extracted trial data included intervention name, therapy type, NSCLC stage, and drug class, and TEAEs. Identified PRO measures were categorized by type (generic vs disease-specific), endpoint designation, and covered concepts (domains/subdomains)
- Trial-level data was analyzed to quantify PRO-inclusive monotherapy trials by year (2015-2026) and by drug class, and to characterize differences in PRO measure use
- PRO measure coverage across disease characteristics and TEAE was qualitatively assessed by mapping domains, subdomains, and item-level concepts to commonly reported symptoms and TEAEs for selected drug class

RESULTS AND DISCUSSION

Figure 2: Trend of PRO Measures Use Over Time (2015-2026)



*Includes EQ-5D-5L, EQ-5D-3L, and EQ-5D-VAS
Trials that included multiple PRO measures were counted more than once for each PRO measure

- Between 2015-2026, a total of 862 US-based NSLCLC trials were identified of which 138 (16%) included PRO measures, exclusively as secondary or exploratory endpoints
- Amongst PRO-inclusive trials, most were ongoing (76%), while 24% were completed; 67 (48.5%) were monotherapy trials
- Use of NSCLC-SAQ was observed following the release of draft FDA Core-PRO Guidance in Cancer Clinical Trials[6]
- PROMIS appeared in NSCLC trials only after 2024, aligning with finalized FDA Core-PRO Guidance[6] **(Fig 2)**
- Use of PRO measures was highest among clinical trials for PD-L1/PD-1 inhibitors (e.g., atezolizumab, durvalumab, nivolumab, and pembrolizumab), followed by ADCs (e.g., dato-DXd) and KRAS inhibitors (e.g., ASP4396, adagrasib), while EGFR inhibitors (e.g., osimertinib, tesavatinib) trials showed comparatively lower PRO inclusion despite higher clinical trials **(Table 1)**
- PRO measures varied substantially in the breadth of concept coverage across NSCLC symptoms and TEAEs, with no single instrument capturing all relevant domains **(Table 1)**
- EORTC QLQ-C30 and NSCLC-SAQ demonstrated the broadest coverage of core NSCLC symptoms and TEAEs across multiple drug classes, while generic measures such as EQ-5D and PROMIS-10 captured functional status and QOL but showed limited specificity **(Table 1)**

Table 1: PRO Measure Concept Coverage Across NSCLC Characteristics and Common TEAEs

PRO Measure and Year of Launch	Domains/Sub-Domains/Items	Core NSCLC Symptoms	ADCs (e.g., dato-DXd)	ALK Inhibitors (e.g., brigatinib, alectinib)	EGFR Inhibitors (e.g., osimertinib, tesevatinib)	KRAS Inhibitors (e.g., adagrasib, sotorasib)	PD-L1/PD-1 Inhibitors (e.g., atezolizumab, avelumab)	TKI Inhibitors (e.g., lenvatinib, zongertinib)
• QLQ-C30 (1988)	Symptoms (Dyspnea, Insomnia, Appetite Loss, Constipation, Diarrhea); Functional Status; Global Health Status; Financial Impact							
• EQ-5D-3L (1990) • EQ-5D-5L (2009) • EQ-5D-VAS (1990)	Pain/Discomfort; Self Care; Mobility; Usual Activities; Anxiety and Depression							
• QLQ-C30-LC-13 (1994)	Symptoms (Coughing, Hemoptysis, Dyspnea, Sore Mouth, Dysphagia, Peripheral Neuropathy, Alopecia, Pain)							
• LCSS (1995)	Symptoms (Appetite, Fatigue, Cough, Dyspnea, Hemoptysis, Pain); Global Measure; Overall Quality of Life							
• PROMIS-10 (2004)	Symptoms; Functional Status; General Mental Health and Emotional Distress; Satisfaction; Overall Quality of Life							
• NSCLC-SAQ (2019)	Pain; Dyspnea; Cough; Fatigue; Appetite							
Trials with PRO Measures*		30	6	21	14	68	13	
PRO-Inclusive Monotherapy Trials		12	4	5	9	13	6	
PRO-Inclusive Monotherapy Trials with Reported Data		1	3	1	2	10	2	

Gastrointestinal: Nausea, Vomiting, Diarrhea, Appetite Loss, Constipation
Fatigue: Fatigue, Asthenia, Malaise
Dermatology: Rash, Alopecia
Neurology: Peripheral Neuropathy
Pain: Musculoskeletal pain, Myalgia, Arthralgia
Respiratory: Cough, Dyspnea, Hemoptysis
Oral: Rash, Mucositis

Trials with PRO measures were counted more than once if combination therapies showed up across different drug classes

Abbreviations: ADC: Antibody Drug Conjugate, ALK: Anaplastic Lymphoma Kinase, CT: Clinical Trials, ED-5D: EuroQOL-5-Dimension, EQ-5D-VAS: EuroQOL-5-Dimension Visual Analog Scale, EGFR: Epidermal Growth Factor Receptor, EORTC-QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, EORTC-QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Lung Cancer, KRAS: Kirsten Rat Sarcoma Viral Oncogene Homolog, LCSS: Lung Cancer Symptom Scale, NSCLC: Non Small Cell Lung Cancer, NSCLC-SAQ: Non Small Cell Lung Cancer Symptom Assessment Question, PD-L1/PD-1: Programmed Death-Ligand 1/Programmed Cell Death Protein 1, PRO: Patient Reported Outcomes, PROMIS: Patient Reported Outcomes Measurement Information System, TEAE: Treatment Emergent Adverse Events, TKI: Tyrosine Kinase Inhibitor, QOL: Quality of Life

LIMITATIONS

- Focusing on US-based trials was intentional to ensure consistency, relevance, and interpretability however, this may limit the generalizability to global NSCLC monotherapy trials and regulatory context

References available on request

CONCLUSION

- **PRO measures remain underutilized in NSCLC monotherapy trials (16%) and are positioned as supportive endpoints**
- **There is no universal standard for PRO measure use across drug classes in NSCLC**
- **PRO measures varied in their concept coverage across NSCLC symptoms and TEAEs, with no single instrument capturing all relevant domains**