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‘Focusing on Core Patient-Reported Outcomes in Cancer Clinical Trials’- Authors Response to Letter

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We thank Grønvold and colleagues for comments on our publication presenting a U.S. regulatory perspective on patient-reported outcome (PRO) data in cancer clinical trials. ¹ In this manuscript we propose to focus our analysis of submitted PRO data on symptomatic adverse events, symptoms of disease, and physical function as a starting point to address calls to incorporate rigorous PRO data in FDA product labeling. Information in FDA product labeling must be generated from well-defined and reliable assessments, and should aim to distinguish the effect of the drug from other influences. ^{2, 3}

Tailoring PRO assessments using a selection of questions from an item library or item bank can provide needed flexibility to address increasing heterogeneity in disease and treatment contexts. We use the PRO version of the National Cancer Institute’s Common Terminology Criteria for Adverse Events (PRO-CTCAETM) and PRO Management Information System (PROMIS[®]) physical function measures as examples of an item library and item bank, respectively. We acknowledge the PRO tools cited in our manuscript and the FDA’s clinical outcome assessment (COA) compendium ⁴ are not the only tools available, and we encourage sponsors to engage FDA early in drug development to discuss their PRO measurement strategy.

Our manuscript does not advocate for analysis of patient-reported symptoms alone. We propose analyzing physical function as a core PRO concept that is important to patients and can capture the tradeoff between disease symptom improvement and symptomatic adverse events. Furthermore, while we propose to focus on three core concepts to analyze for labeling consideration, we are clear that they may not be the only concepts to assess in a

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clinical trial. Other concepts may be needed to address trial objectives, and international drug development stakeholders often request other health-related quality of life domains and/or utility scores to provide supportive data on the broader patient experience.

Similar to Grønvold, we favor a thoughtful combination of static questionnaires and item banks or libraries to create a balanced, flexible and modular approach to PRO assessment to address targeted trial objectives and accommodate the needs of multiple stakeholders. Rigorous PRO collection to minimize missing data and international collaboration toward best practices for trial design and PRO data analysis methods remains critical. As our manuscript states, “the goal should be to achieve a comprehensive evaluation of the patient experience most affected by the therapy, while maximizing the relevance of individual questions and minimizing overall burden and duplication.”

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