Completion rates and trends of the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE®) across 14 oncology clinical trials

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Abstract # 1579

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Background

With growing emphasis on patient-centered regulatory decision making, there is a greater need to incorporate the patient's voice in oncology clinical trials. The FDA, EMA and ICH guidelines are in agreement around the assessment and consideration of the participant voice.[1,2,3] The FDA's 2021 draft guidance on patient-reported outcomes (PROs) for Oncology clinical trials outlines the core PROs to use, which include disease symptoms, physical and role function, overall side effect impact, and symptomatic adverse events (AEs).[3] Further, the new 2023 draft FDA guidance on dose optimization for oncologic treatments acknowledges the benefits of including self-reported symptomatic adverse events to enhance the assessment of tolerability in early phase dose optimization trials.[4] Given the clinical symptoms and disease burden in oncology, patient burden needs to be thoughtfully considered when incorporating PROs into trials. **The present study** assessed trends and feasibility of electronic data collection for symptomatic AEs by analyzing completion compliance and time to complete the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) across 14 oncology trials.

What is the PRO-CTCAE? The PRO-CTCAE is a complementary tool to be used in conjunction with the clinician-reported version. The PRO-CTCAE for a given study can be constructed using a subset of AEs from a library of 78 symptoms that provides a method to assess applicable attributes for each symptom (frequency, severity, amount, presence/absence and/or interference with daily activities).[5] For each symptom, 1-3 attributes are assessed.

Electronic delivery of the PRO-CTCAE can implement conditional branching logic, which reduces participant burden. Electronic delivery of PROs also increases compliance around data collection by preventing missing and inconsistent answers.

Methods

All PRO-CTCAE were collected electronically on Clario Tablets. Operational data for completion status (completed or missed) and duration of time to complete the PRO-CTCAE in seconds was extracted. Completion rates were examined overall and for every 3-month interval (quarters Q1 to Q9+). The median was selected for analyses of time to complete to account for skewness. A linear regression was used to examine time to completion as a function of the number of questions asked to determine the impact of adding questions on completion time.

Results

The sample included 14 studies across Phase I-III trials across a range of cancers **(Figure 1)**. Study durations were 24 weeks and up. The PRO-CTCAE form was completed 13,122 times and missed in 1,182 instances, giving an overall completion rate of 91.7% **(Table 1)**. On average, 25 questions (range 5-47) covered an average of 13 symptoms (range: 4-25). Completion rate was not associated with the number of questions asked **(Figure 2)** or time since enrollment **(Figure 3)**.

The overall median time to complete the PRO-CTCAE was 82s **(Figure 4)** with a study-specific median range of 24s to 276s. Examining time to completion as a function of the number of questions revealed a significant positive association ($F(1,12) = 78.1$, $p<.001$), with an $R2$ of .88. Each additional question added 5.2 seconds to the time it took to complete the assessment **(Figure 5)**.

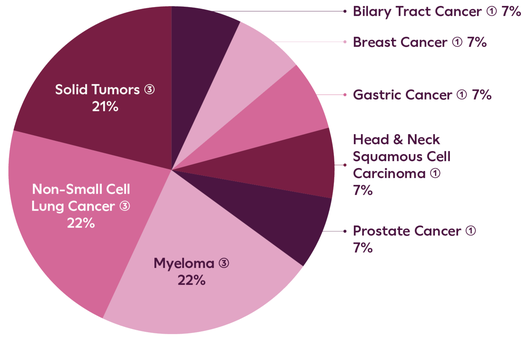

Figure 1. Distribution of oncology indications

PRO-CTCAE Overall Compliance	
% Completed	91.7%
% Missed	8.3%

Table 1. Overall completion rates

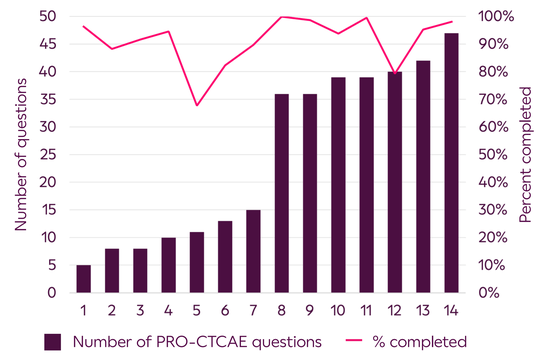

Figure 2. Completion rate by number of questions

This chart shows the number of questions included in the PRO-CTCAE assessment across each of the 14 studies in the bars with labels on the left Y-axis (mean = 25; range 5-47). The completion rate is represented as the line across the top and labels on the right Y-axis. Completion rate was not associated with the number of questions included in the PRO-CTCAE.

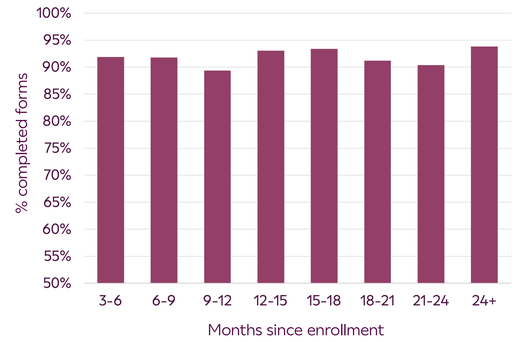

Figure 3. Completion rates over time

This chart shows the percent of completed forms over time. Completion rate was calculated as the number of completed forms divided by the completed plus expected forms for enrolled participants. Months since enrollment is represented on the X-axis in 3-month increments. Completion rate did not change over time.

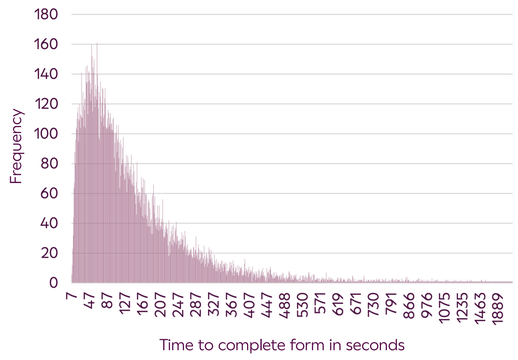

Figure 4. Time to complete form in seconds

This chart shows the frequency of duration for the length of time it took for participants to complete the PRO-CTCAE across studies (Median = 82s; study-specific median range: 24s to 276s).

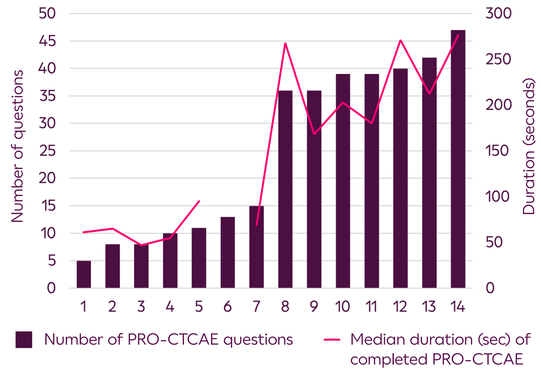

Figure 5. Number of questions by median duration

This chart shows the number of questions represented as the bars and left Y-axis, along with the median duration to complete the form on the line and right Y-axis. As the number of questions included in the PRO-CTCAE increased, the time to complete the PRO-CTCAE increased.

Conclusions

- Completion compliance was high for PRO-CTCAE and remained high regardless of study length and the number of questions included in the PRO-CTCAE form. This suggests that electronic PRO-CTCAE is a feasible solution for collecting self-reported symptomatic AEs.
- Although time to complete the form increased with the number of questions, results suggest that including a higher number of PRO-CTCAE questions does not negatively impact compliance rate.
- Our data showing high completion rates may also reflect the benefits of electronic PROs in reducing patient burden and enhancing data quality, as acknowledged by regulatory agencies.

References

1. The International Council for Harmonisation (ICH) guideline "E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1)" (Nov 2016).
2. The European Medicines Agency (EMA) guideline "Appendix 2 to the guidance on the evaluation of anticancer medicinal products in man – the use of patient-reported outcome (PRO) measures in oncology studies – Scientific guideline (Jun 2014).
3. The U.S. Food and Drug Administration (FDA) guidance document "Core Patient-Reported Outcomes in Cancer Clinical Trials (Jun 2021).
4. The U.S. Food and Drug Administration (FDA) guidance document "Optimizing the Dosage of Human Prescription Drugs and Biological Products for the Treatment of Oncologic Diseases (Jan 2023).
5. The National Cancer Institute (NCI) "Common Terminology Criteria for Adverse Events (CTCAE)" (Version 5.0, Nov 2017).

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