'Focusing on Core Patient-Reported Outcomes in Cancer Clinical Trials' – Letter

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Kluetz *et al.* from the FDA [1] provide a welcome overview of the challenges related to patient-reported outcomes assessment in cancer clinical trials seen from a regulatory perspective.

The article raises a relevant issue in the current era of novel therapies and associated unique adverse events: standardized, so-called "static" questionnaires consisting of a fixed set of items may miss important adverse events.

We agree with many of points made but wish to discuss two proposals from Kluetz *et al.* The first is to use items from the PRO-CTCAE [2] *instead of 'static questionnaires'*. While we concur that the use of a standard library of items such as the PRO-CTCAE may be sensible, we believe that assessment of symptoms alone, rather than a broader set of patients' health experiences, is too restrictive.

Second, Kluetz *et al.* propose, in addition to the PRO-CTCAE, assessing patientreported Physical Function (PF) using the PROMIS instrument. It is unclear why PF is being recommended as the sole functional outcome to be assessed (rather than, say role, emotional or social functioning), and why the PROMIS instrument is being recommended. However robust the psychometrics of this instrument may be, to our knowledge it has yet to be validated for the wide range of language and cultural settings of international trials.

Our recommendation would be to employ a combination of standardized patient-reported questionnaires *and* validated items from item libraries. This would ensure adequate assessment of not only the adverse events of new treatments, but also their impact on the common functional health problems reported by patients.

The EORTC Quality of Life Group has adopted just such an approach, with its "core" QLQ-C30 questionnaire (a computer-adapted testing version and short-forms have also been developed [3]) covering 11 of the 12 core symptoms recommended [4] and condition-specific modules.

Additionally, the EORTC maintains an *Item Library* of 600 items derived from its internationally validated modules, which is available to all interested researchers. Similar solutions and approaches may be available from other groups such as FACIT.

In summary, we view Kluetz *et al.*'s advocacy of specific PRO measures as both premature and without a strong evidence base [5]. There are a number of viable approaches to PRO assessment in cancer trials that address the broad spectrum of relevant patient experience, including both symptoms and functional health, and that are sufficiently flexible for evaluating the effects of new and emerging therapies.

References

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