Review of: "Progression-free survival as a primary end-point: Counting the cost"

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Potential competing interests: No potential competing interests to declare.

In this commentary on the pros and cons of progression-free survival (PFS) as primary endpoint, Ogochukwu Izuegbuna presents the opinion that “an increase in PFS without an accompanying QoL benefits would not be enough approval for a cancer drug.” Of note, this is done using mostly examples of hematological oncology, something that doesn't preclude an appraisal of the work. I believe the author's position is a defendable one in many cases, even though it would be hard to generalize it---for example, to the point of transforming it in a regulatory requirement---in view of the limitations of quality of life (QoL) as primary endpoint in and of itself. Given the multiplicity of results arising from different QoL domains, even if only one instrument is used, and other issues that plague QoL assessment (such as missing data, the potential for multiplicity issues, and discordant results across domains and instruments), it's often difficult to make sense of QoL results as indicative of the overall treatment benefit in a given trial. Nevertheless, I see merit in this position. On the other hand, the article is superficial in the contrast between PFS and overall survival (OS), particularly with regard to the surrogacy issue, something that has been extensively debated in the last two decades. Methodological aspects and key points of view are not addressed, and even the mention of Prentice's criteria---which have long been replaced by the meta-analytical framework---is less than adequate. Another issue I take is with the very title of the article, which mentions cost, even though cost-effectiveness is discussed only in passing and with specific regard to polatuzumab. In that regard, I believe the article can be improved by having an increased focus on the main message, that PFS benefit alone may not be sufficient. Finally, writing can be greatly improved. Some passages are somewhat cryptic, whereas others contain grammatical errors (for an example of the latter, see the sentence between quotation marks above, where the word “benefits” does not accord in number with the article preceding it). With regard to unclear sentences, what is the meaning of “PFS as an endpoint in clinical trials have been muted to have some advantages over OS”? What about “the drug in question should have the same effect as the new surrogate”? Finally, can the author clarify which rate is meant (at which time point) by “with the PFS rate in the Polivy + R-CHP arm being 76.7% (95% CI, 72.7%–80.8%) vs 70.2% in the R-CHOP arm (95% CI, 65.8%–74.6%)”? Despite these criticism, I believe the general argument has merit and deserves wider discussion by the oncology community.