Clinical Trial Development as a Predictor of Accrual Performance—Letter

Anneke T. Schroen

In the November 15, 2010 edition of Clinical Cancer Research, Cheng and colleagues describe an important finding, namely, the association between trial development time and accrual success (1). Their article also reports accrual success rates for NCI Cancer Therapy Evaluation Program (CTEP)-sponsored trials. This publication formally publishes the finding that 40% of cancer clinical trials of all phases close due to poor accrual, which was cited in the Institute of Medicine report "A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program" (2). This statistic has received considerable attention. Cheng’s study also reports that 70.8% of phase III trials result in poor accrual.

These are concerning statistics; however, they rely on a definition of sufficient accrual that is very restrictive for phase III trials and, as a consequence, may overemphasize the problem of poor accrual.

The most important goal of a trial is to answer its intended question. There are several circumstances under which a phase III trial may answer its scientific question without achieving 100% of target accrual. In large trials, closing a few patients short of the intended goal may have no appreciable impact on the statistical power of the study. A study defining successful accrual in phase III trials as 90% or more of target accrual has recently been published (3). Trials may experience greater event rates than anticipated. Trials may close before attaining target accrual for ethically imperative reasons, such as reaching a conclusive finding at interim analysis or closure due to toxicity, both settings in which the scientific question is still addressed. In addition, the study of Cheng and colleagues includes trials still open to accrual, labeling those as successful if they have met 75% or more of target accrual after being open for at least 3 years. Particularly among phase III trials, it is questionable to assume that all trials not meeting this expectation will ultimately fail in accrual.

In quantifying the impact of poor accrual, metrics incorporating the ability of a trial to address the primary endpoint are more reflective of the complexities and variability inherent in real trial conduct than metrics based on meeting accrual targets alone. It would be important to confirm the notable association of accrual success and development time identified here by Cheng and colleagues, using a less restrictive definition of accrual sufficiency. This would serve to bolster our expectations that reducing development time will translate into improved accrual success rates in the future.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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