Survival and Participation in a Cancer Clinical Trial: A Provocative Relationship

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The role of cancer trials in defining the standard of care in oncology is well established. Further, there will be little (if any) debate on the statement that advances in the management of malignant disease are largely the result of appropriately designed and conducted clinical trials. Yet, for several reasons, the current and future relevance of trials to the practice of cancer medicine is undergoing serious challenge.

First, it is recognized that a distressingly low percentage of patients with cancer actually participate in a clinical trial, and inadequate accrual frequently prevents a meaningful answer to the question being addressed [1]. Thus, it is not inappropriate to inquire about the relevance of the results when they are based on such a limited patient sample.

Second, a substantial proportion of cancer studies are designed by the pharmaceutical industry for the purpose of achieving registration. While there is nothing inherently wrong with such sponsorship, it is reasonable to inquire if many of these studies actually address the issues most relevant to practicing oncologists and their patients.

Third, it is increasingly recognized that ‘real-world patients’ (e.g. with older age and presence of comorbidities) are very poorly represented even among the limited patient population who participates in cancer clinical trials. Again, it is necessary to ask if a study whose patients are >10 years younger than the average cancer patient and where common comorbidities (e.g. cardiac, renal, and pulmonary disease and diabetes) are relative or even absolute exclusion criteria provides meaningful data (efficacy and toxicity) for patients actually encountered in ‘routine clinical practice’.

Finally, as oncology quickly moves into the molecular diagnostic era, where decisions are increasingly based on an individual tumor’s ‘molecular signature’, how relevant are ‘phase 3 randomized’ studies that continue to focus solely on the organ of origin of the malignancy?

For the clinical research enterprise to continue to fulfill its essential role in advancing cancer medicine to improve the outcomes of cancer patients, it is reasonable to conclude that appropriate responses are mandated to these challenges. This will surely include essential (and likely substantial) changes to the existing clinical research infrastructure and the acceptance of alternative approaches to both clinical trial design and analysis (including study endpoints).

One factor, which those seeking to support continued reliance on cancer clinical trials can certainly consider, are provocative (but far from conclusive) data suggesting that patients treated on a trial appear to experience superior survival outcomes than patients with management off a clinical study [2]. Of course, there are a number of possible reasons for this observation, prominently including (as previously noted) the often very narrow eligi-
bility for clinical study entry making it extremely difficult to compare the patient populations. It is also obvious that another reason for improved survival may be the benefit that may accrue to patients associated with their being able to receive a new/novel therapeutic regimen.

However, it is also possible that through a patient’s participation in a well-designed and conducted clinical trial, which should include ‘best-practice’ diagnostic, therapeutic, monitoring, and follow-up approaches in a given setting, the chances for as favorable an outcome as possible may be optimized, considering the overriding impact of the underlying clinical status and biology of the cancer in a particular patient.

In this issue of Oncology, Arrieta et al. [3] provide a retrospective review of 1,042 non-small cell lung cancer patients in Mexico treated from January 2007 to December 2014 who were or were not enrolled in a clinical trial. In this interesting and well-documented analysis, enrollment in a clinical trial was associated with superior overall survival.

It will be important for future research in this area to further define the specific role of clinical trials, if any, in optimizing clinical outcomes. Demonstration of such value will certainly provide critical support to those who firmly believe that patient participation in clinical research is also an important strategy to optimize the outcome of clinical care.

References

