In their recent article in the Journal (1), Karrison et al. outline a number of possible advantages of reporting response as a continuous variable (percent change in tumor size) rather than as a dichotomous variable. We agree with them as to the value of reporting response as a continuous variable and would like to suggest some additional possible uses of this approach. We have proposed that plotting percent change in tumor size versus treatment dose might offer increased insight into dose–response relationships and that this might be used to infer predominant resistance mechanisms (2). Furthermore, the relationship of change in tumor size versus dose with the first cycle of therapy may reflect intrinsic resistance mechanisms, whereas the relationship to dose of further change in tumor size with later cycles of therapy may suggest how acquired resistance differs from intrinsic resistance (2). To infer potential major resistance mechanisms, we have used estimated percent tumor cell killing derived from published response rates in assessments of dose–response relationships in non–small cell lung cancer, but we feel that use of percent change in tumor size in individual patients would be preferable if such information were available (3). We have also found that it is feasible to use percent further change in tumor size with each subsequent cycle of therapy to assess the individual impact of each of the four regimens used in...
a randomized alternating strategy to treat non–small cell lung cancer (4).

References

Notes
Affiliation of author: Department of Thoracic/Head and Neck Medical Oncology, University of Texas M. D. Anderson Cancer Center, Houston, TX.
Correspondence to: David J. Stewart, MD, FRCP, Professor of Medicine, Department of Thoracic/Head and Neck Medical Oncology, University of Texas M. D. Anderson Cancer Center, Houston, TX 77030 (e-mail: dstewart@mdanderson.org).
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Response
Dr Stewart agrees that analyzing tumor response as a continuous variable may offer advantages over dichotomizing the endpoint as response or no response. He refers to several interesting papers in which he and coauthors consider how the relationship between change in tumor size and dose could be used to infer chemotherapy resistance mechanisms. We are particularly intrigued with the suggestion that the dose–response relationship during the first cycle of treatment can be examined to derive insights into the initial or “intrinsic” mechanisms of drug resistance, whereas subsequent size changes over later cycles would provide information regarding “acquired” resistance. The types of studies proposed to address these kinds of mechanistic questions may differ somewhat from ours in that more dose levels with fewer patients per dose level would be evaluated (“we propose the use of numerous dose levels and relatively small numbers of subjects per dose”) (1). This is because in the studies proposed by Stewart et al. (1) primary interest centers on the change in the shape of the dose–response curve over multiple treatment cycles. However, the basic idea of gleaning additional information by analyzing tumor size change as a continuous outcome measure is similar.

Theodore Karrison
Michael Maitland
Walter Stadler
Mark J. Ratain

Reference