In Reply

We want to thank Dr. Sorscher for his careful reading and commentary on our paper. With regard to his point about "who benefits" versus who might benefit, we would like to make the following points. Viewpoints in this regard depend on whether one is taking a population-based or an individual-based approach to assessing benefits. Although we readily admit that we may not have perfectly articulated this in the title that we chose for our paper, we were taking a population-based perspective. It is currently not possible, nor will it likely ever be possible, to predict precisely whether a specific treatment will benefit a specific individual. This is true even in diseases like chronic myelogenous leukemia (CML) in which a single mutation drives the disease and there is a highly specific targeted agent available for treatment. Clearly, that intervention has dramatically changed the outcomes for the populations of patients with CML. Most, but not all, people with CML derive benefit from available drug therapy. Knowing about that benefit in populations of individuals with the disease who took that intervention permits an individual and their health care advisors to make an informed choice about whether to take imatinib. The experience of a population has clear utility in assessing the potential for an individual trying to determine if a treatment is right for them.

Dr. Sorscher clearly makes a valid point that patients must be included in the valuing proposition for treatment efficacy. The advocacy community are and clearly need to be involved in trial design and interpretation of study results, particularly in studies conducted by the National Cancer Institute-funded trials conducted by the oncology cooperative groups. In those groups and in studies conducted by industry, we continue to design trials with prespecified and conventional endpoints often based on response rate as well as progression-free and overall survival. Every day, our oncology tracking newsletters and press releases announce that trials have met or failed to meet their primary endpoints. Meeting primary endpoints is just the beginning of the value equation that needs further interpretation weighing toxicity, patient preferences, and societal preferences. For example, it is very common for the U.S. Food and Drug Administration (FDA) to approve a treatment based upon having met prespecified endpoints and then to see European or British regulatory groups turn down authorizing payment for the same drug for the same indication based on a different interpretation of success and value. The FDA does not take monetary cost into consideration in drug approvals. National Institute for Health and Care Excellance (NICE) and the European Medicines Agency (EMA) add that consideration to their valuations. We contend that those valuations should not be a part of the study design but rather of the analyses needed once the study data are available. It is interesting to note that patients outside the U.S. who might want to access a drug based upon a study's result that led to FDA approval of the agent for their indication often cannot access the drug that they want to take regardless of their personal valuation of that agent.

In the end, we believe that careful trial design permits standardized and accurate data reporting, and that allows facts to be interpreted on a case by case basis in making decisions for individual patients. Value determinations for each patient remain the domain of the individual care team interacting with the individual patient and their circle of supporters. We believe that outcomes must be known to be valued. Our discussion on the changing landscape of clinical trial methodology reflects the evolution of how we can and should do that in the face of the availability of more data than was imaginable a half century ago when randomized clinical trials were emerging as the best approach to fact finding. We believe that we now have an opportunity and an obligation to adapt our methodology based on the meticulously documented experiences of the many patients participating in cancer clinical trials over the past 50 years. Our paper supports the notion that we need to take advantage of that opportunity.

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Disclosures

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