From the Editor

Striving to Improve Outcomes in Oncology: Unmet Expectations in a Complex Disease

I have made some progress. Why so late and with such difficulty?  

Paul Cézanne

Parallels between life and art are often drawn, and the words of Cézanne sum up very well our cancer research enterprise, in particular our attempts to deliver better therapies to cancer patients. This issue of CCR Focus deals with several facets of the targeted therapy revolution in oncology. Beginning with imatinib for chronic myelogenous leukemia (CML), our field has embraced the notion that cancer cells can be best managed with therapies aimed at blocking the 1 or 2 signaling pathways that are responsible for maintaining that tumor type. Administering the correct targeted therapy has been termed personalized medicine. However, the latter is more a goal than a reality, and imatinib in CML, as important as it was, likely represents a specific treatment in an incompletely developed malignancy and not a paradigm for all malignancies. Coincident with the development of therapies that would target critical signaling pathways, we also witnessed the endorsement of a second goal—“cancer as a chronic disease.” Unfortunately, we have come to understand that, unlike CML, the majority of cancers are much more complex than we had imagined, a fact underscored by accumulating sequence data, as shown in the Figure 1. On a very practical level, these approaches have left physicians and patients with new agents but unmet expectations.

This issue of CCR Focus examines outcomes—our difficulty in determining true clinical benefit; the increase in clinical trial size that achieves statistical significance without a meaningful advantage; the difficulty in determining a priori the subgroup that will actually benefit, and the subgroup that may be harmed; the importance of recognizing when palliative care is the right choice; the extraordinary costs of some drugs that provide marginal benefit in unselected populations; the critical need for health care reform that supports clinical trials; and the need to maintain equity as we generate ever more expensive therapies. Our guest editors, LoRusso, Wolf, Averbuch, and Schnipper, experts in clinical trials and in ethics, representing both academia and industry, have joined together with a number of experts in the field to summarize these topics in this CCR Focus on marginal outcomes. They urge the community to do more. We hope, as with every issue of CCR Focus, that this issue educates but also stimulates and challenges those working in clinical and translational oncology.

Susan E. Bates
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Fig. 1. Transcriptome sequencing in 24 patients with pancreatic cancer revealed 12 core pathways (A) that contained an average 63 mutations in different genes. Specific genes mutated in tumors from 2 patients are shown (B, C) with the positions on the circle corresponding to the pathways in (A). From Jones et al. (1).

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