Achieving the Goals of Effective, Safe, and Individualized Cancer Care

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At the 2010 Conference on Clinical Cancer Research, held on October 20, 2010, in Washington, DC, co-convened by Friends of Cancer Research and the Engelberg Center for Health Care Reform at the Brookings Institution, participants explored 4 pressing challenges in the field. Articles summarizing the panel’s recommendations on each of these topics are featured in this issue of Clinical Cancer Research (1–4).

Recent years have been marked by numerous important discoveries in clinical cancer research, bringing new therapeutic options to patients in great need. As these discoveries have been translated from bench to bedside, another important trend has emerged: Increasingly, stakeholders across public and private sectors have identified common goals in clinical cancer research and joined together to drive real progress toward safer, more effective, and more individualized cancer prevention, diagnosis, and treatment strategies.

This is a reflection of some important underlying trends in discovery and development. First, collaborative efforts are increasingly required to tackle the most pressing challenges facing clinical cancer research today, including big questions such as how we ensure that drug development is efficient; that resulting products are safe, effective, and personalized as possible; and that regulatory and reimbursement policies facilitate and reward innovation that is valuable to patients. Second, information technology and other types of technical progress have made such collaborations easier. However, many obstacles remain.

Overcoming these obstacles has increasingly been the focus of our collaborative work on innovation in cancer care. October 2010 marked the third year that the Engelberg Center for Health Care Reform at the Brookings Institution and Friends of Cancer Research have convened members of the cancer clinical research community to discuss some of the most significant opportunities and challenges related to their shared goals. With support from the American Association for Cancer Research, the American Society of Clinical Oncology, and Susan G. Komen for the Cure, this conference facilitates substantive multisector collaboration among leading representatives from government, academia, the patient community, and industry. By bringing all of these varied perspectives to the table and organizing expert panels to focus on discrete topics, these conferences have built a track record of producing results. Concepts presented at the 2009 Conference on Clinical Cancer Research led to the publication of 4 articles and stimulated progress on important topics, including ways to streamline data collection for supplemental indications of cancer treatments, use of progression-free survival as an endpoint in phase III oncology trials, development of drug combinations, and an accelerated pathway for approval of targeted cancer treatments (5–8).

One of the most exciting and promising aspects of modern cancer drug development is the potential to personalize treatments by developing drugs that inhibit specific molecular targets. Success stories of personalized cancer treatments include anti–epidermal growth factor receptor (EGFR) therapies, such as erlotinib, which target EGFR-overexpressing tumors, and anti–human epidermal growth factor receptor 2 (HER2) therapies, such as trastuzumab, which target HER2-overexpressing breast cancers. The key to developing such targeted therapies lies in identifying responsive patient populations and tumor characteristics. Due to the molecular heterogeneity of most tumors, however, this has proven extremely challenging. It is often not possible to identify predictive biomarkers before the start of phase III trials of anticancer therapeutics. As a result, many drugs fail to show a statistically robust treatment effect in these trials even though they might be very effective if used in the correct patients. It is clear that new approaches are needed to develop matched diagnostics and therapeutics. The first of the 4 articles developed from presentations at the 2010 conference uses castrate-resistant prostate cancer as a case study to present a potential adaptive phase III trial design in which an appropriate patient population is identified early in the trial, allowing the efficacy of a test therapeutic to be evaluated within that population later in the same trial (1). Such an approach maintains the rigorous statistical standards needed to evaluate drugs, is more consistent with our current knowledge of tumor biology, and can speed progress in getting effective anticancer treatments to responsive patients.

In addition to efficacy, drug safety is a major factor in regulatory decision making. Anticancer drug toxicity can be severe, leading to drug discontinuation or even death, and is often responsible for the failure of a drug candidate to receive marketing approval. Despite the importance of

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safety information in drug development, current methods of preclinical toxicity testing are outdated and rely heavily on animal models that are often not predictive of adverse events in humans. The incorporation of modern systems biology technologies, such as genomics and proteomics, into drug safety testing could greatly improve our evaluation of new drug candidates. Such an approach could enable an understanding of the biology of adverse events, identify biomarkers predictive of specific adverse events, and potentially identify the patients most at risk for an adverse event. The second article presents 2 case studies that demonstrate the potential of systems biology approaches in toxicity testing (2). Integration of these modern techniques into drug safety testing could greatly improve the efficiency and accuracy of drug development.

As treatments for cancer become more effective and patients are living longer, the issue of pain in cancer becomes an increasingly important topic. Cancer-related pain is a frequently reported symptom that can have a significant and long-lasting impact on quality of life. This pain is a frequently reported symptom that can have a significant issue in cancer, integrating pain metrics into clinical and regulatory decision making is challenging due in part to the subjective nature of pain. Furthermore, there is a high level of uncertainty regarding what kind of pain-related data the U.S. Food and Drug Administration (FDA) would find sufficient to contribute to labeling or approval decisions, making many sponsors reluctant to incorporate pain measurements into drug development programs. As a result, few clinical trials include pain palliation or pain prevention as either a primary or secondary endpoint. The third article explores the feasibility of developing objective standards for pain measurement and identifies the need to develop new tools to measure pain (3). Several methodologic challenges need to be addressed in the form of an FDA guidance to facilitate the measurement of pain in oncology clinical trials. Including such measurements and incorporating the resulting information into drug labels would greatly benefit the cancer community, as patients could live not only longer, but happier and more productive lives.

Approval and labeling of new cancer drugs by the FDA relies upon safety and efficacy data from population-based trials. However, data suggest that an average of only 1 in 4 patients receiving an approved cancer drug regimen significantly benefit, whereas the remainder of patients experience little to no benefit and may experience potentially toxic side effects. Although this clearly points to a need for a better understanding of factors associated with treatment response, generating timely and actionable evidence of this sort through prospective clinical trials can be difficult. The fourth and final article uses a case study in non-small cell lung cancer to examine the feasibility of directly engaging patients to participate in a proposed prospective study of molecular determinants of treatment response (4). With a focus on previously marketed drugs, the goal of such a study would be to inform labeling changes and clinical practice such that cancer patients receive treatments that are more personalized and therefore more likely to result in benefit rather than harm.

Each of these articles marks an early but significant step toward resolving real barriers to more effective, safe, and individualized cancer care. More importantly, as a collection, they illustrate the potential for innovation and collaboration within the cancer community and give reason for optimism that these goals can be achieved. To date, the ideas presented have been conceived of and refined by groups of collaborating stakeholders, with the benefit of input from other stakeholders as part of the annual conference. In order for these ideas to continue to come to fruition in a meaningful and practical way, more steps to resolve barriers will be required. In turn, these efforts will require collaboration reflecting active engagement of stakeholders, ranging from patients and consumers to scientists and regulatory officials. We hope to keep working together to make that happen.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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