

## Reflections on 2015

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*Disclosures of potential conflicts of interest may be found at the end of this article.*

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We close a year of remarkable progress in cancer research and care, and make special note of some important trends that this journal is embracing. On the research front, I first would like to recognize two notable achievements that have changed expectations for the future. The first is clustered regularly interspaced short palindromic repeats (CRISPR) technology, which will allow excision of mutant or defective genes and insertion of a physiological alternative. Put simply, we now have the power to remake human DNA. As an example of its potential, this technology could correct inherited disorders that predispose to cancer, or could insert new genes that resist infection by carcinogenic viruses such as HIV, hepatitis B or C, human papillomavirus, or Epstein-Barr virus. Many other applications to cancer are possible. Second, we have witnessed the vast expansion of immunotherapy with checkpoint inhibitors, and the introduction to trial of a series of complementary immunotherapies (vaccines, other checkpoint inhibitors, T-cell and macrophage activators). In the coming year, we expect to learn much more about how to use these expensive drugs more efficiently, developing biomarkers that predict response, and limiting their use to patients who will benefit.

At the same time, we have learned a great deal about targeted therapy and its limitations. Increasingly, we are seeing that tumors are not simple *BRAF* or *ALK* mutants but a collection of subclones that emerge down diverse pathways. Treating the drug-resistant tumor will not be a simple task. We have harvested valuable information from sequential biopsy specimens of primary tumor and have learned that drug resistance is polyclonal, complex, and daunting. Plasma DNA may prove a better picture of the diversity of mutations throughout the body than a biopsy specimen from a single site. Other uses of plasma DNA monitoring are appealing. For example, plasma sampling after local treatment may be able to predict who among adjuvant-treatment candidates is likely to recur after local therapy.

We will be featuring molecular tumor board papers that aid the reader in interpreting results of these and other molecular assays, and in choosing new treatments based on these findings. Despite the enormity of the problem of resistance, the contribution of targeted therapy has been profound, providing treatment options for otherwise incurable tumors.

What about the early trials that fail or lead to equivocal results? These results deserve to see the light of day. I would like to note that our Clinical Trial Results (CTR) section, chaired by Susan Bates and Tito Fojo, continues to provide a much-needed path to publication of early clinical trial results. The failure to publish many valuable trials has awakened the attention of Congress and the National Cancer Institute. There is no reason not to publish these trials, given the support available online from CTR.

We must celebrate the contribution of the Food and Drug Administration and its leadership in adapting to these developments. Nearly 20 new cancer treatments were approved last year, accounting for approximately 40% of FDA's total approvals in 2015, a remarkable number considering the slow progress in the past. Many of these were approved along the new Breakthrough path after only 3 years of testing. It is difficult to understand the anger and denigration expressed by those who would favor unrestrained access to any medicine approved overseas.

I would like to acknowledge the growing interest in community outreach and equity of care. Not all cancer victims in the United States or abroad have access to the molecular tests, targeted drugs, and immunotherapies featured in the scientific papers that grace our journals. There are serious gaps in practice and access to care at home and abroad. Our new section on Community Outreach, chaired by Beverly Moy and Michele Evans, will encourage papers in this emerging area of concern. The rising costs of cancer medicines present a new challenge to patients, physicians, private payers, and governments. Bernardo Goulart, Carlo La

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Vecchia, and Dan Goldstein will address this critical topic—the cost and value of cancer care—in the coming months in a series of papers from noted experts in the field. Likewise, this journal and others have recognized the need to broaden our vision to include global oncology, as the majority of cancer cases and deaths occur in low- and middle-income countries, where cancer diagnosis and care is rudimentary. We invite contributions to all of these new initiatives.

Finally, I would like to thank our reviewers, section editors, and contributors. I hope that we have provided a

valuable forum for publishing the timeliest developments and issues in this fast-changing field of cancer care, in all its dimensions.

#### DISCLOSURES

**Bruce A. Chabner:** Sanofi, Merrimack, Zeltia (C/A, H), BioMarin, Seattle Genetics, Zeltia, Epizyme, Pharmacyclics, Gilead, Celgene (OI), Eli Lilly (ET).

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (ET) Expert testimony; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

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