Journal of the National Comprehensive Cancer Network

Editorial

Personalized Medicine and Breast Cancer Care

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Dr. Burstein's clinical research interests include novel treatments for early- and advanced-stage breast cancer and studies of quality of life and health behavior among women with breast cancer. He has written widely on breast cancer in both traditional medical journals and on the web, including *New England Journal of Medicine* and *Journal of Clinical Oncology*. International committees focusing on cancer treatments that he has or continues to participate in include the NCCN Clinical Practice Guidelines Breast Cancer Panel, St. Gallen Breast Cancer Panel, CALGB Breast Cancer Committee, ASCO Health Services Research and Clinical Research Committees, the National Quality Forum Breast Cancer Technical Panel, and other ASCO expert panels.

"Personalized medicine" has rapidly evolved from connoting cutting-edge thinking about medical care based on individualized need to something of a cliché; everyone wants to focus on personalized medicine these days. At its core, the concept suggests that treatments could be tailored to the health needs of a given person, based on extensive and detailed understanding of the underlying biology of their disease, their intrinsic body function, and the dynamics of whatever intervention is planned. In oncology, the concept is most often linked to 2 particular aspects of personalization: use of gene expression arrays to define which cancer subset most closely describes the tumor, and use of the patient's gene profile to understand either why this cancer developed or how best to treat it.

Breast cancer serves as a model disease for those seeking to develop personalized medicine in oncology. The use of biomarkers and gene expression profiling has yielded important insights into the heterogeneity of breast cancers. We now speak not of "breast cancer" as one monolithic tumor type, but of important, recognizable, definable subsets such as "HER2-positive" breast cancer, "triple-negative" breast cancer, or "ER-positive breast cancer." Further personalization emerges in treatment algorithms. In particular, the ER-positive tumor types are being splintered into subgroups with different treatment needs.

Tumor-based gene expression analyses, such as the OncotypeDX recurrence score, are used to gauge which patients with ER-positive breast cancer should have chemotherapy and which should not. Finally, breast cancer treatment holds the one instance of pharmacogenomic significance in all of cancer medicine—the emerging story of tamoxifen metabolism by the CYP2D6 enzyme and implications of genetic variability at that gene locus on drug effect.

Not surprisingly then, this issue of *JNCCN*, which focuses on breast cancer, carries us far into the realm of personalized medicine. Included in the guideline algorithms are unique treatment recommendations for each tumor subset and clinical decision-making based on individualized assessment of tumor risk for each patient using gene expression assays. The review on tamoxifen and CYP2D6 discusses the strengths of that data and how CYP2D6 testing may emerge as a standardized evaluation for breast cancer patients.

Personalized medicine, however, poses a unique challenge to guideline panels. Historically, guidelines are based on large, randomized clinical trials or meta-analyses. They feature robust scientific and clinical conclusions drawn from cohorts of hundreds if not thousands of patients, and these conclusions are thought to have broad applicability. Those are the hallmarks of "level 1" evidence that are the backbone of treatment recommendations.

Personalized medicine demands a different perspective, based almost by definition on retrospective, subset analyses of large trials or on limited-scale treatment interventions among narrowly defined patient populations. Therefore, we see the demand for much judgment in deciding when a critical mass of data has been accumulated, when a consistent set of scientific observations coalesce, and when the evidence is sufficient to treat one person differently from another. This is the challenge for personalized medicine in oncology—to translate with more style and comprehension the lessons learned from large groups of patients into treatments for individual patients and their cancers—and it is a challenge for guideline developers no less than for patients and clinicians.

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