Speeding Discoveries with Neoadjuvant Studies

Breast cancer trials that focus on giving treatment before surgery broaden understanding of the disease and may lead to better adjuvant trials

“When we give therapy before removing the tumor, we have easy access to good-quality tumor material that can be interrogated with molecular methods, and that information is then correlated with clinical response,” says Carlos L. Arteaga, MD, director of the Breast Cancer Program at Vanderbilt-Ingram Cancer Center (Nashville, TN). “What we learn about treated tumor cells could potentially lead to the discovery of mechanisms of drug resistance and/or new therapeutic targets, and we’re starting with the patient and the actual tumor in question.”

Providing therapy before surgery to shrink tumors, known as neoadjuvant systemic therapy or preoperative therapy, is increasingly common in breast cancer treatment. Because studies have shown that the order of therapy does not affect overall survival, and because neoadjuvant therapy allows quick tracking of a tumor’s response to therapy, investigators are seeking to optimize this approach in trials.

“Neoadjuvant trials allow for better patient selection, leading to smaller trials; they improve our ability to study tumor subsets, biomarkers, and dual-targeted therapies; and they are faster, offering results in months rather than in years,” says Lisa A. Carey, MD, medical director of the University of North Carolina Breast Center.

“In an age when we have a lot of good ideas, neoadjuvant trials may help us triage among them,” she adds. “For example, in HER2-positive tumors, which patients benefit the most from dual targeting? Might some patients forego chemotherapy?”

BROADENING THE SCOPE

Instead of looking at overall or disease-free survival, neoadjuvant trials typically rely on a surrogate endpoint called pathologic complete response (pCR), generally defined in breast cancer as the disappearance of tumor cells in the breast and regional lymph nodes. Many patients don’t respond to therapy, and in these cases better predictive factors are needed. But patients who achieve a pCR tend to have good long-term outcomes.

Results of these trials may help to improve the design of adjuvant trials as well, researchers say. For example, the Neoadjuvant Lapatinib and/or Trastuzumab Treatment Optimization (NeoALTTO) and the Neoadjuvant Study of Pertuzumab and Herceptin in an Early Regimen Evaluation (NeoSphere) trials have already begun to give hints as to the outcomes of corresponding adjuvant trials.

Specifically, NeoALTTO demonstrated that combining the 2 anti-HER2 drugs lapatinib and trastuzumab was better than using a single agent in early breast cancer (Lancet 2012; 379:596–8). More than half of the patients in the combination arm achieved pCR, meaning tissue samples showed no residual cancer cells.

A larger adjuvant companion study—Adjuvant Lapatinib and/or Trastuzumab Treatment Optimization (ALTTO)—is in progress, and if long-term results continue to match
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