

Experts Offer Hope for Patients with Aggressive Breast Cancer

Breast cancer experts from around the country gathered at the sixth annual Oncology Congress in San Francisco, CA, on October 16, 2010, to share recent progress in treating some of the most aggressive forms of the disease.

Dr. Ruth O'Regan from Emory University discussed exciting developments for patients with triple negative breast cancer (TNBC). A subtype lacking expression of the three major molecular targets in this disease (estrogen receptor, progesterone receptor, HER2), TNBC is generally characterized by aggressive behavior and resistance to therapy. In patients with metastatic TNBC, the median survival is only about a year. In summing up current options for these patients, Dr. O'Regan simply said, "We must do better for patients with early TNBC." To this end, she emphasized the need to subtype triple negative tumors to predict patients' risk of recurrence and offer personalized therapy. For example, a subset of patients with TNBC has inactivating mutations in BRCA1 or BRCA2. Loss of BRCA function hinders the ability of the tumor cells to repair certain forms of DNA damage, and sensitizes them to die when treated with drugs that block a second DNA repair enzyme named PARP (poly ADP-ribose polymerase). Dr. O'Regan presented some encouraging results from early phase clinical trials of olaparib, an oral PARP inhibitor, in patients with BRCA mutant breast cancer. Larger trials are underway to assess the effectiveness of PARP inhibitors alone and in combination with chemotherapy for TNBC.

Dr. Scott Christensen from the University of California Davis Cancer Center spoke about recent clinical trials of anti-angiogenic agents in metastatic breast cancer. In particular, he reviewed data on bevacizumab, a monoclonal antibody that recognizes and blocks VEGF-A (vascular endothelial growth factor A), and sorafenib and sunitinib, two small molecule tyrosine kinase inhibitors (TKIs) that target VEGF receptors. In phase III clinical trials, bevacizumab when used as first or second line therapy in combination with chemotherapy improved progression free survival (PFS) and oral response rate (ORR) in patients with metastatic breast cancer. However, the benefits of bevacizumab on PFS in this setting are in the range of 2-3 months. Importantly, the TKIs sorafenib and sunitinib are more toxic, but do not seem to offer any greater PFS benefit over that of bevacizumab in clinical trials so far. One of the big questions discussed was whether or not bevacizumab should be continued after disease progression—a difficult decision for many breast cancer patients and their providers. After summarizing the clinical trials to date, Dr. Christensen offered his position on this issue by saying: "Preclinical models suggest continuation of therapy may be beneficial, but clinical data are lacking." He then alerted the audience to the upcoming RIBBON3 trial, which is designed to specifically evaluate the potential benefits of using bevacizumab beyond progression.

Dr. Paul Goss from the Massachusetts General Hospital discussed the role for extended adjuvant hormonal therapy in breast cancer. He introduced the topic by stating that "breast cancer is a chronic recurring disease." Moreover, Dr. Goss made the point that: "There is no such thing as a trivial recurrence in breast cancer." He summarized data from the ATLAS trial comparing 5 versus 10 years of tamoxifen

therapy, which found not much benefit beyond 5 years. However, he presented more recent clinical trial data showing that node positive breast cancer patients have a significant reduction in risk of death when given extended adjuvant hormonal therapy. Longer duration trials are in progress to address which patients should be offered this extended hormonal therapy and for how long.

Those in attendance were updated not only on where the breast cancer field stands on these challenging issues, but where it is going. The accelerating pace of progress over the past several years certainly gives one hope that targeted therapy will eventually yield benefits even against the most stubborn forms of this disease.