with luminal B compared with luminal A tumors for both histologic subtypes, with patients with ILC deriving greater benefit from adjuvant letrozole compared with those with IDC. Dr. Metzger Filho suggested that clinicians might consider letrozole over tamoxifen for the upfront treatment of patients diagnosed with ILC. However, these results are retrospective in nature and need to be confirmed in other adjuvant aromatase inhibitor trials.

Neurocognitive Impact in Adjuvant Chemotherapy for Breast Cancer Linked to Fatigue: A Prospective Functional MRI Study

Written by Emma Hitt, PhD

Women diagnosed with and treated for breast cancer often experience problems with memory, concentration, and other cognitive abilities that affect their quality of life [Reuter-Lorenz PA, Cimprich B. *Breast Cancer Res Treat* 2013]. Although patients frequently attribute this to chemotherapy, cognitive complaints and deficits have been found before patients undergo any adjuvant treatment [Cimprich B et al. *J Clin Exp Neuropsychol* 2010]. Women treated for breast cancer often report fatigue, but an association between fatigue and neurocognitive function has not been systematically examined. Bernadine Cimprich, PhD, RN, University of Michigan, Ann Arbor, Michigan, USA, presented data from a prospective functional MRI (fMRI) study on the neurocognitive impact of breast cancer-linked fatigue.

Women enrolled in the study were patients with localized breast cancer stages I to IIIa. Twenty-eight patients received adjuvant chemotherapy (anthracycline-based regimen), 37 received radiotherapy alone without chemotherapy, and 32 age-matched healthy controls were enrolled. At 2 time points coinciding with pre- and 1-month postchemotherapy assessments, participants performed a verbal working memory task with varying levels of demand for cognitive control while undergoing fMRI scanning. Participants provided self-reports using the Attentional Function Index and the Functional Assessment of Cancer Therapy-Fatigue during these assessments.

Cognitive domains that may be affected in cancer patients include attention, working memory, processing speed, and executive function [Wefel JS, Schagen SB. *Curr Neurol Neurosci Rep* 2012]. Error rates on a verbal working memory task were significantly higher ($p<0.05$) before treatment in the chemotherapy and radiation groups compared with the healthy group.

In addition, fMRI scanning revealed that inferior frontal gyrus functioning differed between patients and controls over time ($F=3.88$, $p=0.05$). Left inferior frontal gyrus activation at the pretreatment evaluation was related to an increase in fatigue over time.

The group receiving chemotherapy had significantly higher fatigue levels both before and after treatment ($p<0.01$). However, higher levels of fatigue across all groups were associated with reduced cognitive function over time. In addition, preadjuvant treatment brain alterations during the working memory task were able to predict severity of post-treatment fatigue. Thus, fatigue and pretreatment neural vulnerability are contributors to cognitive problems in patients with breast cancer and may further compound any cognitive effects of chemotherapy.

Dr. Cimprich said, "'Chemo brain' is not an appropriate label for cancer-related cognitive dysfunction [and]... early interventions to reduce psychological distress may improve cognitive function over the course of treatment."

ATLAS: 10 Versus 5 Years of Adjuvant Tamoxifen in ER-Positive Disease

Written by Emma Hitt, PhD

Treatment with tamoxifen for 5 years has substantially reduced the risk of breast cancer recurrence and death throughout the first 15 years after diagnosis of estrogen receptor (ER)-positive early breast cancer [Early Breast Cancer Trialists' Collaborative Group (EBCTCG). *Lancet* 2011]. The Adjuvant Tamoxifen: Longer Against Shorter [ATLAS] trial compared the effects of continuing tamoxifen for a total of 10 years with stopping after the standard 5 years of treatment. Richard Gray, MSc, University of Oxford, Oxford, United Kingdom, presented data from the ATLAS trial on the effect of tamoxifen on 15-year survival [Davies C et al. *Lancet* 2012].

Women with ER-positive breast cancer (n=6846) who had received 5 years of adjuvant tamoxifen treatment were randomized to continue tamoxifen for another 5 years or to stop at Year 5 (control). Breast cancer recurrence, any other new primary cancer, compliance, hospital admissions, and cause of death were recorded during annual follow-up exams, with a median follow-up of 8 years.

Compliance to treatment was ~80%. During the trial, 617 women in the 10-year tamoxifen group experienced a recurrence compared with 711 women in the 5-year tamoxifen group ($p=0.002$). Breast cancer mortality during