Susan G. Komen
Research Grants – Fiscal Year 2014

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A trial of endocrine response in patients with invasive lobular carcinoma

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Public Abstract:

How do patients with invasive lobular breast cancer (ILC), who represent 5-15% of breast cancer patients as a whole, differ from those with invasive ductal breast cancer (IDC)? Is their prognosis different? Do their tumors respond differently to medical treatments? The answers to these questions are disturbingly unclear due to a void of research on this topic. The current standard is to treat ILC patients no differently than IDC patients, despite numerous studies that suggest inherent differences in these tumor types. Recent data suggest that patients with ILC may actually respond differently to endocrine therapy than those with IDC. In an analysis of the BIG 1-98 trial presented by Dr. Metzger and colleagues at the 2012 San Antonio Breast Cancer Symposium, patients with ILC had proportionally worse outcomes on tamoxifen versus letrozole, an aromatase inhibitor (AI), in comparison to patients with IDC. These findings are compellingly similar to what my collaborators in the Oesterreich laboratory have found in a cell line model of ILC, which also exhibited a resistance to tamoxifen and a particular sensitivity to fulvestrant, a drug that is currently only used to treat stage IV (metastatic) breast cancer. We have therefore designed a clinical trial to study response to tamoxifen, anastrozole (an AI), and fulvestrant in the tumor tissue of women with newly-diagnosed ILC. The patients will be randomized to one of three different therapies in a 21-day window of time before their breast cancer surgery or pre-surgical medical therapy. Changes in proliferation (growth rate) markers in their ILC breast tumor tissue will be studied before and after treatment, as these changes are known to be predictive of patient response to therapy. We believe this work is critically important, especially as ILC incidence has significantly increased in the last two decades. If it were considered as an independent cancer type, (instead of a subtype of all breast cancers), ILC would rank as the sixth most common cancer in women, as common as non-Hodgkin lymphoma or melanoma. Identifying a biological signature of tamoxifen or AI-resistance and/or fulvestrant-sensitivity in ILC would have dramatic implications for the future management of patients with this breast cancer subtype. Currently, endocrine therapy after an early-stage breast cancer diagnosis follows a "one-size-fits- all" approach, with most premenopausal women receiving tamoxifen, and most postmenopausal receiving AIs. If our trial indicates that these treatments are less effective in comparison to fulvestrant at decreasing proliferation (growth rate) of ILC, it would warrant a much larger trial in patients with ILC to confirm these findings. As fulvestrant is already approved for treatment of stage IV (metastatic) breast cancer, this trial could be rapidly mounted, and a positive result could lead to more effective treatment for the 25,000-30,000 patients diagnosed with ILC in the United States annually.