

Current Issues in Breast Cancer

In the United States, 1 in 8 women will be diagnosed with breast cancer in her lifetime. This is a frightening statistic, but insights into the prevention and treatment of breast cancer have greatly expanded the armamentarium that we can bring to bear on this disease. For example, research has provided us with the ability to identify individuals who carry a genetic predisposition for breast cancer. Anti-hormonal agents beyond tamoxifen now play a major role in the treatment and maybe soon in the prevention of hormone-responsive breast cancer. Some of these advances are reviewed in the series of articles included in this issue of *Cancer Control*.

In the first paper, Michael Baum, ChM, FRCS, discusses the three trials evaluating the benefits and potential risks of aromatase inhibitors for early-stage hormone-responsive breast cancer. For several decades, tamoxifen was the “lone ranger” for adjuvant hormonal therapy. However, initial results from three large randomized trials evaluating the adjuvant use of aromatase inhibitors have recently been reported. The ATAC trial compared anastrozole and tamoxifen or a combination of the two for 5 years; the NCIC trial studied letrozole compared with placebo in patients who completed 5 years of tamoxifen; and the MA-17 trial compared 5 years of tamoxifen with 2 years of tamoxifen followed by 3 years of exemestane. All of these trials demonstrated benefit from the aromatase inhibitor in terms of disease-free survival. However, due to limited follow-up time or early trial stopping, no overall survival data are available and the long-term risks from treatment may not be completely assessable. Furthermore, these trials do not establish whether the benefits are due to a specific aromatase inhibitor or whether the aromatase inhibitors are interchangeable. We are therefore left with several unanswered questions: Which aromatase inhibitor is most beneficial and least harmful? Which sequence of drugs provides the optimal results?

Natalie G. Coburn, MD, and colleagues then evaluate the incidence of ductal carcinoma in situ and invasive cancer, as well as tumor size and stage, the rate of breast conservation surgeries, and the overall survival in a well-screened population. Using data from the Rhode Island Cancer Registry from 1987 to 2001, they show that compared to the years 1987-1989, the rate of screening mammography in the years 1999-2001 increased for residents of Rhode Island women of all ages. Over the same time period, while the incidence of cancer remained stable, the median tumor size decreased from 2 cm to 1.6 cm, and

fewer cases presented as advanced-stage disease. This was associated with a decrease in breast cancer mortality and a higher rate of breast conservation. This study supports other larger studies suggesting an important role of screening mammography. Similar to reports from other larger studies, the decrease in mortality was most evident in women between 50 and 64 years of age. In younger women, there was a trend for decreased mortality that did not reach statistical significance.

In a retrospective literature review, Solange Pendas, MD, and coauthors discuss the controversial role of sentinel lymph node biopsy for ductal carcinoma in situ (DCIS) and the assessment of the sentinel lymph node rather than surrounding lymph nodes before and after exposure to neoadjuvant chemotherapy. They present arguments to justify sentinel lymph node biopsies for DCIS. The diagnosis of DCIS poses a sufficient risk for occult or missed invasive disease and local recurrence, and benefits thus outweigh the minimal risks of sentinel lymph node sampling. To date, however, there is insufficient information available to determine the optimal timing and method to assess the nodal status of patients undergoing neoadjuvant chemotherapy. Prospective studies to address this issue are warranted.

Fortunately, over the last few years, we have learned more about the genetic behavior of breast cancer. Healthcare providers often discuss the risks and benefits of genetic testing with individuals in high-risk groups or in families where women are diagnosed at a young age or where other family members are affected. However, the information is complex, and the time spent with patients and families is often limited. Furthermore, the Internet provides our patients with a vast amount of information, but much of it is more confusing than useful, and some of it is incorrect. Genetic testing can be a powerful tool when used properly; a positive test may lead to a more extensive and often invasive prophylactic approach such as bilateral mastectomy and oophorectomy. In contrast, a negative test result in an individual with an affected family member who carries a gene mutation may provide assurance by indicating that her risk of breast and ovarian cancer is similar to that of the general population.

Kimberly Kelly, PhD, and coworkers investigate the benefits of genetic counseling in a group of individuals with genetic mutations resulting in an increased risk of breast and other cancers. The authors found that genetic counseling leaves even highly educated individuals better

equipped in dealing with the complexity of *BRCA1* and *BRCA2* mutations in terms of the risks for developing breast and other associated cancers. Hayley S. Thompson, PhD, and colleagues present the outcomes of two studies assessing patient education materials that describe the genetic risk of developing breast cancer. Despite continued efforts to improve the readability of these materials, many patients, particularly those with low health literacy skills, still have difficulty understanding them. Continued efforts are needed to develop and promote materials that are more easily understood and more user-friendly.

Also included in this issue is a radiology feature that describes a rare abnormality of the breast that can mimic benign or malignant tumor. This article enlightens us on its clinical, radiologic, and pathologic findings.

The articles in this issue of *Cancer Control* focus on just a few of the recent discoveries in breast cancer research. A major current focus is the better understanding of molecular pathways that promote tumor proliferation and early metastasis and the development of targeted therapies of this disease. Furthermore, observations from limited studies suggest that environmental stimuli and behavior patterns such as the higher prevalence in sedentary lifestyles and the increase in obesity may also influence the incidence of breast cancer. These findings may shape the approach to breast cancer in the near future.

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