# National Institutes of Health

## *Fact Sheet* *Breast Cancer*

### Thirty Years Ago

- Approximately 75% of women diagnosed with breast cancer survived their disease at least 5 years.
- Mastectomy was the only accepted surgical option for breast cancer treatment.
- Only one randomized trial of mammography for breast cancer screening was completed. Several others and the joint National Institutes of Health (NIH) and American Cancer Society (ACS) Breast Cancer Detection Demonstration Projects were just beginning.
- Clinical investigation of combination chemotherapy, using multiple drugs with different mechanisms of action, and of hormonal therapy as post-surgical (adjuvant) treatment for breast cancer was in its earliest stages.
- Hormonal treatment of inoperable or advanced breast cancer with tamoxifen, a selective estrogen receptor modulator or SERM, was under investigation but not yet approved by the Food and Drug Administration (FDA).
- The genes associated with an increased risk of breast were unknown.

### Today

- Nearly 90% of women diagnosed with breast cancer will survive their disease at least 5 years.
- Breast-conserving surgery (lumpectomy) followed by local radiation therapy replaced mastectomy as the preferred surgical approach for treating women with early stage breast cancer.
- Routine mammographic screening is an accepted standard for the early detection of breast cancer. The results of eight randomized trials and of the Breast Cancer Detection Demonstration Projects established that mammographic screening can reduce mortality from breast cancer.
- Combination chemotherapy became standard in the adjuvant treatment of women with early stage breast cancer. The goal of this systemic therapy is to eradicate cancer cells that may have spread beyond the breast. Neoadjuvant chemotherapy, or chemotherapy given before surgery to reduce the size of the tumor and to increase the chance of breast-conserving surgery, is being studied in clinical trials.
- Hormonal therapy with SERMs, such as tamoxifen, and aromatase inhibitors is now standard in the treatment of women with estrogen receptor-positive breast cancer, both as adjuvant therapy and in the treatment of advanced disease. Estrogen receptor-positive breast cancer cells can be stimulated to grow by the hormone estrogen. SERMS interfere with this growth stimulation by preventing estrogen from binding to its receptor. In contrast, aromatase inhibitors block estrogen production by the body. FDA-approved aromatase inhibitors include anastrozole, exemestane, and letrozole.
- Clinical trials demonstrated that Tamoxifen and another SERM, raloxifene, prevent the development of invasive breast cancer in women at high risk of this disease. Tamoxifen is approved by the FDA as a breast cancer prevention drug.
- The monoclonal antibody trastuzumab is effective in treating breast cancers that overproduce a protein called epidermal growth factor receptor 2 or HER2. This protein is overproduced in about 20% of breast cancers. These HER2-overproducing cancers tend to be more aggressive and are more likely to recur. Trastuzumab targets the HER2 protein, and this antibody, in conjunction with adjuvant chemotherapy, can lower the risk of HER2-overproducing breast cancer recurrence by 50% compared to chemotherapy alone.
- The study of large groups of related individuals (kindreds) led to the identification of several breast cancer susceptibility genes, including *BRCA1*, *BRCA2*, *TP53*, and *PTEN/MMAC1*. Mutations in *BRCA1* and *BRCA2* account for approximately 80-90% of all hereditary breast cancers, and women who carry mutations in these genes have a lifetime risk of breast cancer that is roughly 10-times greater than that of the general population.

### Tomorrow

We will exploit our rapidly increasing knowledge of genetics, molecular biology, and immunology to develop even more effective and less toxic treatments for breast cancer. We will expand our ability to target and disrupt the effects of molecular changes that cause breast cells to become cancerous. In addition, we will use this knowledge to personalize breast cancer therapy. For example:

- Gene expression analysis has led to the identification of five subtypes of breast cancer that have distinct biological features, clinical outcomes, and responses to chemotherapy. This knowledge should allow the development of treatment strategies based on an individual's tumor characteristics.

- A patient's response to chemotherapy is influenced not only by the genetic characteristics of their tumor but also by inherited variation in genes that affect a person's ability to absorb, metabolize, and eliminate drugs. This knowledge should allow prediction of tumor response to and the likelihood of severe adverse effects from individual chemotherapy drugs or classes of drugs and facilitate development of personalized therapies. It should also aid in the design of more effective and less toxic chemotherapeutic agents.