The National Surgical Adjuvant Breast and Bowel Project (NSABP)

The National Surgical Adjuvant Breast and Bowel Project (NSABP) is one of the cooperative clinical trials groups funded largely by the U.S. National Cancer Institute. For almost 50 years, the work of the NSABP has led to reducing the extent of surgical procedures and improving outcome for patients with early-stage breast cancer through the conduct of large randomized clinical trials that evaluated various aspects of local and systemic therapy.

On April 4, 1958, the first patient was enrolled in the first randomized clinical trial conducted by an organization which was to become the National Surgical Adjuvant Breast and Bowl Project (NSABP). Today there are 200 member institutions with 700 satellite centers located throughout the United States, Canada, Puerto Rico, and Ireland. The NSABP was among the first research groups to recognize the importance of including community-based investigators among its members. Today the majority of participating sites are located at non-university centers, allowing patients the opportunity to enter NSABP clinical trials without the burden or cost of travel to academic centers. More than 5,000 surgeons, medical oncologists, radiation oncologists/pathologists, nurses, clinical research assistants (CRAs), and other medical professionals participate in NSABP trials.

In 1967, Dr. Bernard Fisher was named the chairman of the group and in 1970 the group’s headquarters were moved to the University of Pittsburgh, beginning the ‘modern’ era of the NSABP. Over the next 25 years, Dr. Fisher’s leadership catapulted the NSABP to the forefront of clinical cancer research. Since 1971, more than 76,000 patients have entered NSABP trials, and 43,835 are still in active follow-up. The current NSABP chairman is Dr. Norman Wolmark (Professor of Human Oncology at the Drexel University College of Medicine and Chairman of the Department of Human Oncology at Allegheny General Hospital). Joseph Costantino, DrPH, is the Director of the NSABP Biostatistical Center at the University of Pittsburgh. The Group’s Operations Center and Biostatistical Center are both located in Pittsburgh. In 1995 the NSABP incorporated as the NSABP Foundation, Inc., a 501C3 not-for-profit foundation, and in 1999 the foundation became the grantee for the Operations Center.

Breast Cancer Clinical Trials

Among the best known NSABP clinical trials are those that have evaluated local-regional therapies for invasive and non-invasive breast cancer. The results of these trials that were initiated and completed in the 1970s and 1980s (NSABP B-04, B-06, and B-17) have been instrumental in changing the paradigm of surgical management of both invasive and non-invasive breast cancer that previously was based on Halstedian principles of tumor growth and dissemination. In the late 1990s the NSABP returned to its surgical roots with the design and conduct of the NSABP B-32 trial that compared sentinel node biopsy to conventional axillary dissection in clinically node-negative breast cancer patients. More recently, the NSABP, in collaboration with RTOG, designed and is currently conducting protocol B-39, that compares conventional whole breast irradiation with accelerated partial breast irradiation in patients with stage 0, I and II breast cancer.

In parallel to the studies of loco-regional therapy, the NSABP designed and conducted several landmark clinical trials of adjuvant systemic therapy. These trials had a profound impact in establishing adjuvant chemotherapy and adjuvant tamoxifen as standards of care for patients with node-positive and node-negative breast cancer. In addition, they established a role for tamoxifen in patients with ductal carcinoma in situ (B-24). Recent results of another NSABP landmark trial (B-31) established the value of trastuzumab in patients with HER-2 neu positive breast cancer.
In the late 1980s, the NSABP initiated the landmark B-18 trial, the largest trial to evaluate neoadjuvant chemotherapy in patients with operable breast cancer. This trial set the foundation for the use of neoadjuvant chemotherapy in this setting and for the conduct of several other landmark neoadjuvant trials evaluating additional chemotherapeutic agents (B-27) and biologic targeted therapies such as bevacizumab and lapatinib (B-40 and B-41).

More recently conducted adjuvant trials by the NSABP have evaluated the worth of aromatase inhibitors in patients with DCIS (B-35) and as extended adjuvant therapy in patients with invasive breast cancer (B-33) and the worth of bisphosphonates in the adjuvant setting (B-34). Ongoing adjuvant trials evaluate optimal duration of anthracyclines in node-negative breast cancer (B-36) and optimal duration of aromatase inhibitors in patients with ER-positive breast cancer (B-42).

In 1992, NSABP expanded its research agenda to include the concept of chemoprevention. Since that time, the group has completed two large breast cancer chemoprevention trials (P-1 and P-2) that screened more than a quarter million women and randomized over 33,000 healthy individuals at increased risk for the future development of breast cancer. Both trials evaluated selective estrogen receptor modulators (first tamoxifen and subsequently raloxifene) for reducing invasive breast cancer risk. The results of these trials eventually lead to the approval of both tamoxifen and raloxifene by the U.S. Food and Drug Administration as methods for reducing breast cancer risk in women at high-risk for the disease. The NSABP currently maintains a large repository of annotated tumor specimens (over 70,000) from all the NSABP trials, in the form of paraffin blocks. This repository has proven an invaluable resource for the conduct of multiple translational research studies under the leadership of Dr. Soon Paik. Most notably, based on paraffin blocks from the B-14 and B-20 trials, the NSABP has played a major role in the development and validation of the 21-gene recurrence score assay (OncotypeDX), used for prognosis and prediction of chemotherapy benefit in node-negative estrogen receptor-positive breast cancer. Plans for future NSABP trials include the evaluation of trastuzumab in combination with breast irradiation in patients with HER2 overexpressing DCIS following lumpectomy, the evaluation of anti-angiogenic therapy with sunitinib in patients who have residual disease in the breast and/or axillary nodes after neoadjuvant chemotherapy, and the evaluation of trastuzumab in patients with invasive breast cancer and low/equivocal levels of HER2 expression.

Eleftherios P. Mamounas, Chair, Breast Committee, National Surgical Adjuvant Breast and Bowel Project, Pittsburgh, PA

D. Lawrence Wickerham, Associate Chairman, National Surgical Adjuvant Breast and Bowel Project, Pittsburgh, PA