Tamoxifen reduced the incidence of breast cancer in women at high risk in the NSABP-P-1 and IBIS-I trials. NSABP-P-2 (the STAR trial) compares another SERM (raloxifene) to tamoxifen in that setting. Data from the ATAC trial — demonstrating an advantage to anastrozole over tamoxifen in reduction of contralateral cancers — hint toward the future use of aromatase inhibitors in a chemoprevention setting, such as the recently launched IBIS-II trial comparing anastrozole to a placebo. The widespread utilization of screening mammography has led to a dramatic increase in the number of women diagnosed with DCIS. NSABP trials B-17 and B-24 demonstrated a stepwise improvement in local and contralateral tumor control with the use of breast radiotherapy and tamoxifen in women who underwent a lumpectomy. NSABP-B-35 and IBIS-II will compare anastrozole to tamoxifen in postmenopausal patients with DCIS.

Tamoxifen lowered the risk of invasive breast cancer by 40% (odds ratio 0.60 [0.45–0.79]), with a significant effect in invasive cancer, and it’s highly likely they will impact DCIS as well. We know that the majority of DCIS lesions are likely to be ER-positive. Craig Allen has shown that age-per-age, tumor for tumor, DCIS is even more likely to be ER-positive than invasive cancer. If that’s true, then we have even more reason to be optimistic about the studies of aromatase inhibitors in DCIS.

The NSABP study comparing tamoxifen and anastrozole for patients with DCIS is essentially a trial aimed at preventing invasive breast cancer. Aromatase inhibitors have emerged as good agents for the treatment of metastatic breast cancer, both second- and first-line, and the pivotal results from the ATAC trial demonstrated adjuvant anastrozole was more effective than tamoxifen in reducing recurrence rates and contralateral breast cancers. If patients with DCIS fail, it’s usually in the ipsilateral or contralateral breast rather than in the regional nodes or distant sites. Aromatase inhibitors are well tolerated in general. In the ATAC trial, the safety profile of anastrozole was impressive. Patients had fewer thromboembolic events, endometrial cancers and menopausal symptoms than with tamoxifen, but with aromatase inhibitors we need to monitor bone density and fractures.

CSSR-IBIS-II-B-26, EU-202203
NSABP-B-35, CTSU, AGO5, NSABP-B-33, NCCTS-NSABP-B-23, SWOG-NSABP-B-35
No. of patients
Tamoxifen Placebo Hazard ratio
CT (clinical depression) 0.50-0.92
NSABP-P-1 AND IBIS-I STUDIES: BREAST CANCER EVENTS
Tamoxifen alone or in combination trial and the design of IBIS-II (the second Chemoprevention and Management of DCIS

NSABP-P-1 and IBIS-I studies: breast cancer events

CLINICAL TRIALS OF AROMATASE INHIBITORS IN DCIS
NSABP-B-35 and IBIS-II are important trials, both comparing anastrozole and tamoxifen in postmenopausal patients with DCIS. In our experience with large numbers of patients, aromatase inhibitors are better tolerated than tamoxifen. Despite the results of the randomized trials, patients complain of weight gain on tamoxifen. Others include hot flashes, menopausal symptoms and possibly a low level of clinical depression. Patients also worry about endometrial cancer and blood clots. With aromatase inhibitors, some antralgias are reported, but these agents are very well tolerated.

Aromatase inhibitors have already proven to have a significant effect in invasive cancer, and it’s highly likely they will impact DCIS as well. We know that the majority of DCIS lesions are likely to be ER-positive. Craig Allen has shown that age-per-age, tumor for tumor, DCIS is even more likely to be ER-positive than invasive cancer. If that’s true, then we have even more reason to be optimistic about the studies of aromatase inhibitors in DCIS.

INCIDENCE OF INVASIVE BREAST CANCER FOLLOWING RALOXIFENE THERAPY IN POSTMENOPAUSAL WOMEN WITH OSTEORPOROSIS: MORE AND CORE TRIAL DATA


SELECT PUBLICATIONS


Tamoxifen is highly selective for ERα at the nanomolar level. Dose-finding study of anastrozole in postmenopausal women with aromatase inhibitors. Br J Cancer 2003;89:1343-51.


