Four randomized prospective trials have evaluated tamoxifen for chemoprevention of breast cancer. The National Surgical Adjuvant Breast and Bowel Project (NSABP) P-1 trial reported that tamoxifen reduced the risk of invasive breast cancer by 49%. Two smaller European trials, the Royal Marsden Hospital Chemoprevention Trial and the Italian Tamoxifen Prevention Study, demonstrated no decrease in the incidence of breast cancer among women using tamoxifen. The International Breast Cancer Intervention Study confirmed that tamoxifen can reduce the risk of breast cancer in healthy women. The Multiple Outcomes of Raloxifene Evaluation trial, which evaluated the use of raloxifene (Evista) to prevent osteoporosis, found that the risk of invasive breast cancer decreased by 76%. A uniform theme in these trials is that tamoxifen reduces the risk of breast cancer among women at high risk for the disease. Tamoxifen is currently approved for breast cancer risk reduction. However, because of the side effects associated with its use (i.e., endometrial cancer and thromboembolism), other agents are being investigated. The Study of Tamoxifen and Raloxifene is designed to compare the efficacy of tamoxifen and raloxifene in reducing breast cancer risk. Aromatase inhibitors will also be studied in the setting of chemoprevention for breast cancer.

Chemoprevention can be defined as the use of specific natural or synthetic chemical agents to reverse, suppress, or prevent the progression of premalignant lesions to invasive carcinoma.[1,2] Tamoxifen is classified as a first-generation selective estrogen-receptor modulator (SERM). It is a proven treatment for breast cancer, which has encouraged its testing as a chemopreventive agent in healthy women.[3] Four randomized prospective clinical trials have used tamoxifen as a chemopreventive agent for breast cancer. Two of the trials—the NSABP P-1 study and the International Breast Cancer Intervention Study (IBIS-I)—did demonstrate a reduction in breast cancer risk with tamoxifen. The Royal Marsden Hospital Chemoprevention Trial, a pilot study for the IBIS-I trial, and the initial analysis of the Italian Tamoxifen Prevention Study revealed no decrease in the incidence of breast cancer among women using tamoxifen. Raloxifene (Evista) is a second-generation SERM that prevents loss of bone mineral density. The Multiple Outcomes of Raloxifene Evaluation (MORE) trial was originally designed to determine whether raloxifene reduced the risk of fracture in postmenopausal women with osteoporosis, with the incidence of breast cancer as a secondary end point. In this article, we review data from each of these five studies and discuss the differences among the trials (Table 1). Breast Cancer Prevention Trial In 1992, the National Cancer Institute in collaboration with the NSABP launched the Breast Cancer Prevention Trial (BCPT, P-1).[4] The primary aim of this double-blind, placebo-controlled, randomized clinical trial was to determine whether tamoxifen administered for 5 years prevented invasive breast cancer in women at increased risk. Eligible women were age 60 or older, were age 35 to 59 with a 5-year predicted risk of breast cancer of at least 1.66%, or had a history of lobular carcinoma in situ (LCIS). Risk was estimated using the Gail model,[5] which considers current age, age at menarche, age at first live birth, number of first-degree relatives with breast cancer, and the number of breast biopsies ever performed. A previous diagnosis of atypical hyperplasia doubles the estimated risk. Between June 1, 1992, and September 30, 1997, 13,388 women entered the trial and were randomly assigned to receive tamoxifen at 20 mg/d or placebo. Almost all the participants were white (96.4%), more than one-third (37.1%) had had a hysterectomy, and more than one-half (56.8%) had one first-degree relative with breast cancer. The trial was stopped in March 1998, and results were reported, because statistical significance had been achieved in a number of study end points.
Trial Results

The median follow-up time was 54.6 months. Through July 1998, a total of 368 invasive and noninvasive breast cancers developed among the 13,175 women with evaluable end points. The overall risk of invasive breast cancer was reduced by 49%. There were 175 cases of invasive breast cancer in the placebo group compared with 89 in the tamoxifen group (risk ratio = 0.51; 95% confidence interval [CI] = 0.39-0.66; \( P < .00001 \)). The annual rate of invasive breast among women taking tamoxifen was 3.4 per 1,000 women, compared with 6.8 per 1,000 women taking placebo. The risk of invasive breast cancer was reduced in all groups in the trial. For noninvasive breast cancer, risk was reduced by 50%, with 69 cases in women receiving placebo and 35 in those receiving tamoxifen (\( P < .002 \)). The average annual rate of noninvasive breast cancer per 1,000 women was 2.68 in the placebo group compared with 1.35 in the tamoxifen group. The BCPT showed that tamoxifen confers a substantial net benefit in women with a diagnosis of either LCIS or atypical hyperplasia. For women with a history of LCIS, the reduction in risk was 56% (risk ratio = 0.44; 95% CI = 0.16-1.06), and for women with a history of atypical hyperplasia, risk was reduced by 86% (risk ratio = 0.14; 95% CI = 0.03-0.47). Tamoxifen reduced the incidence of estrogen-receptor-positive tumors by 69%, but there was no difference in the incidence of estrogen-receptor-negative tumors. The incidence of osteoporotic fractures involving the hip, spine, and radius was reduced by 19% among women taking tamoxifen (111 events vs 137 events in the placebo group), and the 45% reduction in fractures of the hip missed reaching statistical significance because of the small number of events reported. Adverse Effects

Women who received tamoxifen had a 2.53 times greater risk of developing invasive endometrial cancer than did women who received placebo (95% CI = 1.35-4.97). The average annual rate per 1,000 women was 2.30 in the tamoxifen group and 0.91 in the placebo group. The increased risk was seen predominantly among women aged 50 and over (in women 49 or younger, the risk ratio was 1.21 with a 95% CI = 0.41-3.60; in women older than 50, the risk ratio was 4.01 with a 95% CI = 1.70-10.90). All cases of invasive endometrial cancer that occurred among women receiving tamoxifen were classified as stage 0 or I according to the International Federation of Gynecology and Obstetrics (FIGO). The number of thromboembolic events increased among women taking tamoxifen, particularly those aged 50 years and older. The event rate for pulmonary embolism reached statistical significance. The rate of cataract development increased marginally (by 14%) in women taking tamoxifen who were free of cataracts at the time of study entry. The only symptomatic differences between the placebo and tamoxifen group were bothersome hot flashes and vaginal discharge. Bothersome hot flashes were reported by 46% of women in the tamoxifen group compared with 29% in the placebo group. Moderately bothersome or worse vaginal discharge was reported in 29% of women in the tamoxifen group compared with 13% of those in the placebo group. This randomized clinical trial provided the first information to support the hypothesis that breast cancer can be prevented in women at increased risk for the disease. **Italian Tamoxifen Prevention Study** The Italian Tamoxifen Prevention Study was initiated in October 1992.[6] This double-blind placebocontrolled, randomized trial evaluated tamoxifen in healthy women aged 35 to
70 years. In view of the potential side effect of endometrial cancer, the study was restricted to women who had undergone a hysterectomy. Recruitment for the study started in October 1992 and ended in July 1997. The trialist and data-monitoring committee decided to end recruitment primarily because 26% of women dropped out of this study; 5,408 women were randomized to receive tamoxifen at 20 mg/d or placebo for 5 years. Among the 5,378 women with complete data, 48.3% had a bilateral oophorectomy, and 18.2% had at least one first-degree relative or an aunt with breast cancer. Women were allowed to take hormone replacement therapy (HRT) while participating in the study. The primary end points were reduction in the frequency and mortality of breast cancer. At a median follow-up of 46 months, 41 cases of breast cancer were reported-19 among women in the tamoxifen arm and 22 among women in the placebo arm ($P = .6$). The number of deaths from vascular disease were lower than expected from the Italian national rates. A subgroup analysis that was not part of the original protocol revealed a protective effect for tamoxifen among women who took HRT during the study period. At the time that the initial results were reported, the conclusion was that tamoxifen did not confer a significant protective effect against breast cancer in women at normal or slightly reduced risk of the disease. Also, women who were using HRT benefited from the administration of tamoxifen.

**Study Update**

An update of the Italian Tamoxifen Prevention Study was reported in 2002.[7] At an extended median follow-up of 81.2 months, 79 cases of breast cancer had been identified. Breast cancer was diagnosed in 45 of 2,708 women receiving placebo and 34 of 2,700 women receiving tamoxifen (odds ratio = 0.76; 95% CI = 0.47-1.60). The difference was not statistically significant ($P = .215$). Among women who took HRT during the trial, the cumulative frequency of breast cancer was 0.92% (0.17-1.66) in the tamoxifen group and 2.58% (1.30-3.85) in the placebo group. Among women who used HRT either at baseline or during the study, breast cancer was diagnosed in 17 of 791 receiving placebo and 6 of 793 receiving tamoxifen ($P = .022$). The update supported the trial's original conclusion that tamoxifen provides some benefit in the prevention of breast cancer, but the difference was nonsignificant in women with a normal or slightly reduced risk of the disease. The results also suggest that tamoxifen seems to reduce the risk of breast cancer in women who use HRT compared with nonusers of HRT.

**Subgroup Analysis**

In a subgroup analysis, Veronesi et al.[8] were able to identify a group of women at increased risk for estrogen-receptor-positive breast cancer. This group consisted of women taller than 160 cm (the median height of the overall study cohort), with at least one functioning ovary, who had reached menarche no later than age 13, and who had no full-term pregnancy before age 24. This group of 702 (13%) women was classified as high risk. The remaining group of 4,693 (87%) women was classified as low risk. Information on required baseline characteristics was missing for 13 women. In the high-risk group, the risk of breast cancer was increased threefold over that in the low-risk group (hazard ratio = 3.32; 95% CI = 1.78-6.17). Tamoxifen reduced the incidence of breast cancer in the high-risk group ($n = 3$ vs $n = 15$ in the placebo group, $P = .003$); however, it had no effect in the low-risk group (tamoxifen = 31, placebo = 30; $P = .89$). It is important to emphasize that this subgroup analysis was not used as a stratification factor at the time of randomization. Thus, these findings need to be confirmed in randomized prospective trials.[9]
Royal Marsden Hospital Chemoprevention Trial
The Royal Marsden Hospital Chemoprevention Trial was initiated in 1986 as a preliminary pilot study for IBIS-I.[10,11] The aim of this randomized, placebo-controlled chemoprevention trial was to assess whether tamoxifen would prevent breast cancer in healthy women at increased risk for the disease based on family history. Each participant had at least one first-degree relative under age 50 with breast cancer, one first-degree relative with bilateral breast cancer, or one affected first-degree relative of any age and another affected first-degree or second-degree relative. Women were allowed to take HRT during this study. Between October 1986 and April 1996, 2,494 women between the ages of 30 and 70 were randomized to receive tamoxifen at 20 mg/d or placebo for up to 8 years. The primary end point was the occurrence of breast cancer. The median follow-up was 70 months, and 2,471 of the women were analyzed. A total of 70 invasive and noninvasive breast cancers occurred among the women in this trial. The frequency of breast cancer was the same for women receiving tamoxifen or placebo (tamoxifen = 34, placebo = 36; relative risk = 1.06; 95% CI = 0.7-1.7), and there appeared to be no interaction between the use of HRT and the effect of tamoxifen on breast cancer occurrence. A total of 12 cases developed among 523 women who received HRT while on tamoxifen, compared with 13 of 507 women receiving placebo ($P = .6$). An update of this trial[12,13] reported 75 cases of breast cancer in the placebo group compared with 62 in the tamoxifen group (odds ratio = 0.83; 95% CI = 0.58-1.16).

International Breast Cancer Intervention Study
Between April 1992 and March 2001, 7,152 women aged 35 to 70 years and at high risk for breast cancer were enrolled in the IBIS-1 trial and randomized to receive tamoxifen at 20 mg/d for 5 years or placebo.[14] Eligible women had risk factors for breast cancer indicating at least a twofold relative risk among those aged 45 to 70 years, a fourfold relative risk among those aged 40 to 44 years, and a 10-fold relative risk among those aged 35 to 39 years. Approximately 60% had two or more first-degree relatives with breast cancer; one-third of women had previously undergone hysterectomies. Use of HRT was permitted, and approximately 40% of women used such therapy at some point during the trial. The primary end point was the incidence of breast cancer, including ductal carcinoma in situ (DCIS). **Trial Results**

A total of 7,139 women were included in the analysis. At a median follow-up of 50 months, 170 breast cancers had been diagnosed (including DCIS). The rate was 32% (95% CI = 8%-50%) lower in the tamoxifen group than in the placebo group (tamoxifen = 69, placebo = 101; $P = .01$). The risk of developing estrogen-receptor-positive invasive tumors was reduced by 31%, but there was no reduction in the risk of estrogen-receptor-negative tumors. Among women taking HRT during the trial, 38 cases of breast cancer occurred in the placebo group and 29 in the tamoxifen group (odds ratio = 0.76; 95% CI = 0.47-1.23). Among women who received HRT before the trial only, 21 cases of breast cancer developed in the placebo group and 9 in the tamoxifen group (odds ratio = 0.43; 95% CI = 0.20-0.91). A nonsignificant twofold increase in the incidence of endometrial cancer was found in the tamoxifen group (tamoxifen = 11, placebo = 5; odds ratio = 2.20; 95% CI = 0.80-6.06). The

**Table 2**

<table>
<thead>
<tr>
<th>Population</th>
<th>Number Randomized</th>
<th>Intended Duration of Treatment</th>
<th>Number of Breast Cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postmenopausal women with osteoporosis</td>
<td>7,705</td>
<td>4 yr</td>
<td></td>
</tr>
</tbody>
</table>

*Numbers for 2 dose levels of raloxifene combined.

DCIS = ductal carcinoma in situ; MORE = Multiple Outcomes of Raloxifene Evaluation.
women enrolled in this trial were at moderately increased risk of developing breast cancer, with 60% of the study cohort having a 10-year risk ranging from 5% to 10%. Participation in the trial required at least a twofold relative risk for breast cancer for women aged 45 to 70 years, a fourfold relative risk for women aged 40 to 44 years, and a 10-fold relative risk for women aged 35 to 39 years. Risk factors used included a combination of family history, lobular carcinoma in situ, atypical hyperplasia, nulliparity, and benign breast biopsies. The IBIS-I investigators used a model to predict the absolute 10-year risk of developing breast cancer, but the details of their model have not been published. In contrast, 44% of the women in the NSABP BCT had greater than a 3% 5-year risk of developing breast cancer, as determined using the validated Gail model.[5] Among women enrolled in the BCPT, tamoxifen reduced the risk of breast cancer by 34% in high-risk women without either atypia or LCIS, which is nearly identical to the 32% reduction in risk seen in the IBIS-I study. Although there was no overall difference in the effect of tamoxifen among women who used HRT compared with those who had never used HRT, tamoxifen did reduce the incidence of breast cancer in women who had used HRT before enrollment in IBIS-I. This reduction is remarkably similar to the findings in the Italian tamoxifen study. In IBIS-I as in the Italian trial, tamoxifen produced a differential effect based on the status of participants’ use of HRT. Women who used HRT during the trial achieved a 24% reduction in the risk of invasive breast cancer with tamoxifen use, similar to the 27% reduction observed among women who had never used HRT; women who had used HRT only before initiating tamoxifen therapy (and not during the trial) had a statistically significant 57% reduction in the risk of breast cancer. 

**Adverse Events**

All the women in the IBIS-I trial who developed endometrial cancer were postmenopausal at diagnosis. Most of the endometrial cancers occurred in women older than age 50 at the time of randomization. All were FIGO stage I except for one case in the placebo group that was stage II. The rate of thromboembolic events was 2.5 times greater in the tamoxifen group than in the placebo group (95% CI = 1.5-4.4; P = .001), and 42% of these events occurred within 3 months of surgery or after periods of immobility. There were no differences in the number of cerebrovascular accidents, myocardial infarctions, or other vascular events between treatment groups. A significant excess of deaths from all causes occurred in the tamoxifen group (25 vs 11, P = .028). This increase in mortality is of concern, but is not statistically rigorous due to the multiple, unplanned comparisons in the analysis. In summary, IBIS-I confirmed that tamoxifen can reduce the risk of breast cancer in healthy women. Temporary cessation of tamoxifen should be considered during and after major surgeries or periods of immobilization to reduce the risk of thrombosis, according to the investigators. **Multiple Outcomes of Raloxifene Evaluation** The Multiple Outcomes of Raloxifene Evaluation (MORE) was a multicenter, randomized, double-blind trial designed to determine whether 3 years of raloxifene therapy reduced the risk of fracture in postmenopausal women with osteoporosis.[15] Women were also monitored for breast cancer, a secondary end point. The trial was initiated in 1994, and a total of 7,705 women who were at least 2 years postmenopausal and no older than age 80 were enrolled. Participants had osteoporosis defined by the presence of vertebral fractures or a femoral neck or spine T-score of at least 2.5 SDs below the mean for young healthy women. Women who were taking estrogens during the previous 6 months were excluded, and 12.3% of women reported a family history of breast cancer. Participants were randomized to receive raloxifene at 60 or 120 mg or placebo.

**Trial Results**

At a median follow-up of 40 months, 54 cases of breast cancer were confirmed among the 7,705 women originally enrolled in the study. Of these, 40 cases were invasive cancer, 12 were DCIS, and 2 had insufficient information available to classify the degree of invasion (1 in the 60-mg group and 1 in the 120-mg raloxifene group). There were 27 cases of invasive breast cancer in the placebo group compared to 13 cases in the raloxifene group (relative risk = 0.24; 95% CI = 0.13-0.44; P < .001). There were 12 cases of DCIS-5 in the placebo group and 7 in the raloxifene group. The reduction in the risk of invasive cancer was similar for both the group taking raloxifene at 60 mg/d (relative risk = 0.22; 95% CI = 0.10- 0.50) and the group receiving the 120-mg/d dose (relative risk = 0.26; 95% CI = 0.12-0.56). Raloxifene reduced the risk of invasive estrogenreceptor- positive breast cancer by 90% (relative risk = 0.10; 95% CI = 0.04-0.24) but did not reduce the risk of estrogen-receptor-negative breast cancer (relative risk = 0.88; 95% CI = 0.26-3.0). In addition, the agent was associated with statistically significant increases in the incidence of hot flashes, influenza-like syndromes, endometrial cavity fluid, and leg cramps. The risk of venous thromboembolic disease was 3.1 times higher (95% CI = 1.5-6.2) in women receiving raloxifene than in women receiving placebo. Raloxifene did not increase the risk of endometrial cancer (relative risk = 0.8; 95% CI = 0.2-2.7). Investigators of the study concluded that 3 years of treatment with raloxifene decreases the risk of invasive breast cancer by 76% in postmenopausal women with
osteoporosis. **Four-Year Results**

Four-year results from the MORE trial have now been reported[16] and are summarized in Table 2. A 3-year treatment phase was extended to 4 years after the trial was initiated. During the 4-year trial, raloxifene reduced the incidence of all types of breast cancer by 62% (relative risk = 0.38; 95% CI = 0.24-0.58), and of invasive breast cancer by 72% (relative risk = 0.28; 95% CI = 0.17-0.46). The incidence of invasive estrogen-receptor-positive cancers also decreased compared with placebo (relative risk = 0.16; 95% CI = 0.09-0.30), but had no effect on estrogen-receptor-negative tumors (relative risk = 1.13; 95% CI = 0.35-3.66). These results are consistent with results based on the 3-year follow-up. The MORE trial was not designed to evaluate invasive breast cancer as a primary end point. In addition, women in the MORE trial were at lower risk of breast cancer compared with women in the BCPT.[2] Further study of raloxifene is indicated. This agent may have a better safety profile than tamoxifen, leading to greater efficacy and fewer endometrial cancers. At this time, however, raloxifene cannot be recommended for chemoprevention outside of a clinical trial.[12]

**Differences in the Tamoxifen Chemoprevention Trials**

Before the results of the BCPT were submitted for publication in 1998, the results of the Royal Marsden and Italian studies had been published. Both of these smaller European trials failed to confirm the findings of the NSABP study. Subsequently, an updated report from the Italian Tamoxifen Prevention Study also found a reduction in the incidence of estrogen-receptor-positive breast cancer among an important subgroup of women. The results of the IBIS-I study were reported in September 2002, and they confirmed that tamoxifen can reduce the risk of breast cancer in healthy women. Based on the results of the BCPT, the US Food and Drug Administration approved the use of tamoxifen for breast cancer risk reduction in women aged 35 years or older, with a 5-year risk of 1.66% or greater.[4] The reason for the approval, despite the Royal Marsden and Italian data, was a full scientific review of the nature of the European trials. Numerous methodologic differences existed between the BCPT and European trials in terms of trial design, trial implementation, and characteristics of the women studied. These differences made it very likely that both the Royal Marsden and Italian trials would fail to detect an overall effect for tamoxifen among the populations that were studied. Both these trials were statistically less powerful[17] and smaller than the BCPT, with fewer person-years of follow-up and fewer reported events. Moreover, the risk of breast cancer among women in these trials was lower than in the BCPT.[4] The US Preventive Services Task Force found the evidence from the BCPT sufficiently convincing to conclude that tamoxifen confers substantial benefit.[18] After a comprehensive review of the literature, the American Society of Clinical Oncology's technology assessment working group concluded that tamoxifen may be offered to reduce the risk of breast cancer in women with a defined 5-year projected risk greater than or equal to 1.66%.[12] Risk/benefit models and clinical trials suggest that tamoxifen provides the greatest clinical benefit with the fewest side effects in younger (premenopausal) women.[19] This population is less likely to develop either thromboembolic events or uterine cancer. Tamoxifen also confers the greatest clinical benefit with minimal side effects in women who do not have a uterus and in those at higher risk of breast cancer.[12] **Overview of Combined Results**

In January 2003, Cuzick et al.[13] published an update of available data and an overview of the combined results of the breast cancer prevention trials. The tamoxifen prevention trials showed a 38% (95% CI = 28%-46%; P < .0001) reduction in the incidence of breast cancer and a 48% reduction in the incidence of estrogen-receptor-positive cancers (95% CI = 36%-58%; P < .0001). However, there was no reduction in the incidence of estrogen-receptor-negative breast cancers (hazard ratio = 1.22; 95% CI = 0.89-1.67; P = .21). Age had no effect on the degree of breast cancer reduction. The rates of endometrial cancer increased in all the tamoxifen prevention trials (consensus relative risk = 2.4; 95% CI = 1.5-4; P = .0005), but no increase in endometrial cancer was observed with the use of raloxifene. Most of the excess risk occurred in women older than age 50. Venous thromboembolic events were increased in all the tamoxifen prevention studies (relative risk = 1.9; 95% CI = 1.4-2.6; P < .0001). Similar results were also seen in the MORE trial. Overall, there was no effect on all-cause mortality in the tamoxifen prevention trials (hazard ratio = 0.90; 95% = 0.70-1.17; P = .44). The authors concluded that the evidence clearly shows that tamoxifen can reduce the risk of estrogen-receptor-positive breast cancer. An emerging theme from the tamoxifen prevention trials is that tamoxifen reduces the risk of breast cancer in a population of women who are considered at high risk for the disease. However, because of the side effects of tamoxifen, new agents are being explored. New approaches are also needed to prevent estrogen-receptor-negative breast cancers. **STAR Trial**

The findings from the BCPT and MORE trials led the NSABP to design and implement its second breast cancer prevention trial, P-2, the Study of Tamoxifen and Raloxifene (STAR).[1,20] The primary aim of the STAR trial is to determine whether
(1) compared with tamoxifen, raloxifene significantly reduces the incidence of invasive breast cancer, (2) compared with raloxifene, tamoxifen significantly reduces the incidence of invasive breast cancer, or (3) the statistical superiority of one of the treatments cannot be demonstrated, and the choice of therapy should be based on risk/benefit considerations. Additional primary objectives include an evaluation of the incidence of noninvasive cancer, endometrial cancer, cardiovascular events, and bone fractures. The trial was launched in July 1999 in both the United States and Canada.

**Study Design**

The STAR trial is restricted to postmenopausal women whose projected 5-year risk of developing invasive cancer is 1.66% or higher as determined by the Gail model. Eligible women include those aged 35 or older with no prior history of invasive breast cancer or DCIS. Postmenopausal women with a history of LCIS who are age 35 or older are also eligible. Through February 28, 2002, 12,637 women were randomized for participation. More than 58% of the randomized participants have 5-year Gail model risk scores greater than or equal to 3%. [20] A total of 19,000 high-risk eligible women will be enrolled and randomized to receive tamoxifen at 20 mg/d or raloxifene at 60 mg/d for 5 years. The STAR trial is scheduled to report outcomes in 2007. [12] Until those results are available, it is inappropriate to use raloxifene for the purpose of reducing the risk of breast cancer.

**Aromatase Inhibitors**

Evidence is accumulating that the third-generation aromatase inhibitors are as effective or more effective than tamoxifen for the treatment of established breast cancers. New agents such as the aromatase inhibitors are associated with significantly fewer side effects of endometrial cancer and thromboembolism. [21] A new IBIS trial (IBIS II) has been proposed for women with an increased risk for breast cancer because of family history. This trial will randomize 10,000 high-risk postmenopausal women to either tamoxifen at 20 mg/d, the aromatase inhibitor anastrozole (Arimidex) at 1 mg/d, or placebo, and another 4,000 women to tamoxifen or anastrozole. [3, 22]

**Conclusions**

The chemoprevention trials have taught us that tamoxifen should not be used indiscriminately in all women as a means to reduce breast cancer risk. The risk of breast cancer and the characteristics in the population of women being evaluated will influence the extent of benefit achieved. [23] Many large populations of women at high risk for breast cancer who could potentially benefit from chemopreventive therapy can be identified through the use of available benefit/risk assessment methodology. [19] Two issues must be addressed when considering tamoxifen for the prevention of breast cancer. The first concerns who is expected to benefit from the drug based on their membership in the target population. The second is to what extent the observed risks compete with the potential benefits for an individual. [19] Health-care providers who counsel women about tamoxifen should ensure that patients make a fully informed decision. A risk assessment should include a description of the benefits and risks of tamoxifen therapy as they relate to the individual patient. [24, 25]

**Disclosures:**

The author(s) have no significant financial interest or other relationship with the manufacturers of any products or providers of any service mentioned in this article.

**References:**


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