

Breast Cancer Chemoprevention

Women at increased risk for developing breast cancer are good candidates for considering treatment with chemoprevention agents.

Chemoprevention is the use of natural, synthetic, or biological chemical agents to reverse, suppress, or prevent either the initial development or the progression of cancer.

Currently, there are two chemoprevention agents that are Food and Drug Administration (FDA) approved for risk reduction in women at increased risk of breast cancer; tamoxifen and raloxifene. Studies show that these two medications effectively reduce the risk of breast cancer in women at increased risk. Additional studies are looking at a newer class of drugs

Breast Cancer Statistics In Women

- * About **184,450** cases of breast cancer were diagnosed in 2008
- * About **40,480** deaths due to breast cancer occurred in 2008
- * A woman's lifetime risk of breast cancer is approximately 1 in 8 (**12%**)
- * Average age at breast cancer diagnosis is **64**
- * The 5-year survival rate for women diagnosed with breast cancer is **87.3%**
- * The 10-year survival rate for women diagnosed with breast cancer is **79.9%**
- * In Vermont, about **482** breast cancer cases are diagnosed each year
- * In Vermont, about **96** deaths due to breast cancer occur each year

called aromatase inhibitors to determine if they reduce risk. Herbs and dietary supplements are also being studied.

Tamoxifen

Tamoxifen (Nolvdex) is an oral medication used to treat and prevent breast cancer. Tamoxifen, a selective estrogen-receptor modulator (SERM), works by blocking estrogen. Tamoxifen inhibits estrogen from binding to receptors on cells in the breast, thereby reducing its ability to fuel the growth of breast cancer cells. Tamoxifen is FDA approved as a breast cancer prevention agent for women 35 and older at increased risk for developing breast cancer.

Tamoxifen has been used for more than 30 years to treat breast cancer by reducing the risk of in-breast cancer recurrence and decreasing the development of cancer in the opposite breast. The Breast Cancer Prevention Trial (BCPT) was initiated in the 1990's to investigate the role of tamoxifen in reducing the risk of breast cancer among women at increased risk for the disease. The BCPT trial randomized over 13,000 women at increased risk for breast cancer to re-

ceive either 20 mg of tamoxifen or placebo daily for 5 years. Women were followed for 7 years. The study found:

- Tamoxifen reduced the risk of invasive breast cancer by 43%.
- Tamoxifen reduced the risk of ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS) by 37%.

The IBIS-I study, an international clinical trial that began in 1992, followed more than 7,000 women at increased risk for breast cancer and found that tamoxifen decreased the risk of estrogen receptor-positive breast cancer by about 34% compared to those taking a placebo.

More recent findings from the IBIS-I study have shown that the risk reduction effect of tamoxifen continued beyond

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Tamoxifen continued

the 5 years the drug was actually taken. In fact, the risk-reducing effects of tamoxifen were shown to last for at least 10 years.

Along with reducing the risk of developing breast cancer, tamoxifen can also help prevent osteoporosis. The BCPT trial found that tamoxifen reduced the risk of bone fractures of the hip, wrist, and spine by about 32%.

Although the benefits of tamoxifen use in women at increased risk for breast can-

cer are clear, there are potential risks and side effects. Tamoxifen may increase one's risk for endometrial (lining of the uterus) cancer, stroke, deep vein thrombosis and pulmonary embolism. Some research suggests tamoxifen may also increase one's likelihood of developing cataracts. Women taking tamoxifen have reported the following side effects: hot flashes and vaginal discharge.

Raloxifene

Like tamoxifen, raloxifene (Evista) is a SERM and blocks the effects of estrogen on the breast tissue, reducing the likelihood of developing breast cancer. Raloxifene can also help prevent osteoporosis. Unlike tamoxifen, raloxifene does not increase one's risk of developing endometrial cancer. Raloxifene is FDA approved as a breast cancer prevention agent in postmenopausal women at increased risk for developing breast cancer and to prevent and treat osteoporosis in all postmenopausal women.

The CORE trial, a large research study looking at the rate of breast cancer in 5,213 postmenopausal women taking raloxifene or placebo for 8 years, found that raloxifene reduced the rate of invasive breast cancer by more than 50% compared to the placebo. Subsequently, the Study of Tamoxifen and Raloxifene (STAR) trial randomized over 19,000 post-

menopausal women at increased risk for breast cancer to tamoxifen or raloxifene treatment for 5 years. The study found raloxifene to be equal to tamoxifen in preventing invasive breast cancer. However, raloxifene did not significantly reduce the rate of LCIS or DCIS.

Although raloxifene may not be as effective as tamoxifen in reducing the risk of non-invasive breast cancer, it appears to have a better side effect profile. The STAR trial reported that women taking raloxifene fare better regarding side effects and risk of blood clots (raloxifene users had 30% fewer blood clots than tamoxifen users). Common side effects associated with raloxifene include: hot flashes, vaginal dryness, leg cramps, flu-like symptoms and swelling. The STAR trial found the hot flashes and vaginal side effects to be more common in the tamoxifen group than in the raloxifene group.

Aromatase Inhibitors

Aromatase Inhibitors (AIs) are used to treat and prevent breast cancer from recurring in postmenopausal women. AIs work by blocking aromatase from changing androgens into estrogen, thereby lowering estrogen levels in the body and reducing the ability of estrogen receptor-positive breast cancer to grow.

AIs include anastrozole (Arimidex), exemestane (Aromasin), and letrozole (Femara). AIs are FDA approved for use in postmenopausal women to treat or prevent the recurrence of breast cancer and research shows AIs to be better at doing

so than tamoxifen. Clinical research trials are currently underway to determine the role of AIs as breast cancer chemoprevention agents.

These trials include the British IBIS-II study comparing anastrozole to placebo in 6,000 postmenopausal women at increased risk of breast cancer and the Canadian MAP.3 study comparing exemestane to placebo in 4,560 postmenopausal women at increased risk of breast cancer. The MAP.3 trial is enrolling women locally at UVM/FAHC. To learn more about this study contact Fonda Kingsley at 802-656-8502.

Summary of Tamoxifen Versus Raloxifene

	Tamoxifen	Raloxifene
FDA Approved For	<ul style="list-style-type: none"> Breast cancer prevention in premenopausal and postmenopausal women over 35 years of age who are at high risk for breast cancer 	<ul style="list-style-type: none"> Breast cancer prevention in postmenopausal women at high risk for breast cancer. Preventing and treating osteoporosis in postmenopausal women
Benefits	<ul style="list-style-type: none"> Reduces risk of invasive and noninvasive¹ breast cancer Can help prevent osteoporosis 	<ul style="list-style-type: none"> Reduces risk of invasive breast cancer Can help prevent osteoporosis
Risks	<ul style="list-style-type: none"> Increases risk for endometrial cancer Increases risk for blood clots² May increase risk of cataracts 	<ul style="list-style-type: none"> Increases risk for blood clots²
Side Effects	<ul style="list-style-type: none"> Hot flashes Night sweats Vaginal discharge Genital itching Leg cramps 	<ul style="list-style-type: none"> Hot flashes Vaginal dryness or irritation Leg cramps Flu-like symptoms Swelling in the hands or feet

¹ Noninvasive breast cancer includes DCIS and LCIS

² Major blood clots include stroke, deep vein thrombosis (DVT) and pulmonary embolism (PE)

Aromatase Inhibitors continued

The safety profile of AIs appears more favorable than that of tamoxifen and raloxifene. AIs are not associated with serious blood clots or endometrial cancer. However, AIs are more likely to speed up osteoporosis and may cause more bone fractures. AIs are generally well tolerated; the main side effects are muscle and joint discomfort, headaches, hot flashes and vaginal dryness.

Breast Cancer Chemoprevention at the Vermont Cancer Center

- **MAP.3**– Exemestane (AI) vs. Placebo in postmenopausal women
- **Statin Study**– Lipitor vs. Placebo in premenopausal women
- **Vitamin D Study**– Vitamin D vs. Placebo in women with dense breasts (*forthcoming*)
- **AACT Trial**— Counseling to increase exercise in women 2-36 months after breast cancer treatment

For more information contact Fonda Kingsley at 802-656-8502.

Other Potential Agents

Other agents being investigated to better understand their ability to reduce breast cancer risk include aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs); statins (cholesterol lowering drugs); and vitamin D. These agents are appealing because they are generally well tolerated with few risks and side effects.

Some research suggests that aspirin and NSAIDs may decrease risk of breast cancer, but findings are inconclusive. The ability of statins and vitamin D to reduce breast cancer risk appears promising, but

additional research is needed before stronger conclusions can be made.

Researchers of the High Risk Breast Program are currently investigating the role of statins on breast density and are planning a randomized trial of vitamin D versus placebo to look at breast density and breast cancer risk. For more information on either of these studies contact Fonda Kingsley at 802-656-8502.

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HIGH RISK
BREAST
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Winter 2009

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Roasted Butternut Squash Soup

Adaptation of Chef Michael Kloeti's (of Michael's on the Hill Restaurant) recipe .

Ingredients:

2 ounces Onion, yellow, diced
3 ounces Celery Root, peeled and diced
3 ounces Parsnip, peeled and diced
3 ounces Apples, Granny Smith, peeled, cored and diced
1 ½ pounds Butternut Squash, peeled, seeded and diced
1 ½ ounces Maple Syrup
4 cups Water or chicken stock
8 ounces Vermont Apple Cider
1/2 pound of Bacon, julienne cut
2 tablespoons of Crème Fraiche
pinch Cinnamon, ground
to taste Salt and fresh ground black pepper
6 tablespoons Sharp Cheddar, grated
2 tablespoons Butter, unsalted, melted
2 teaspoons Chives, chopped

Method for the soup:

1. Roast vegetables and apple at 375° F until golden brown--about 25 minutes.
2. Add the apple cider, water and maple syrup to the roasting vegetables.
3. Bring to a boil, and reduce the heat. Cook about 10 minutes until extremely soft.
5. Season to taste with salt and pepper
6. Puree.
7. Mix the crème fraiche, cinnamon and salt and pepper together.

Method for the bacon:

1. Cook slowly over low heat until bacon is crisp. With a slotted spoon, remove bacon from the pan onto a paper towel-lined plate to absorb excess fat.
2. To serve, pour hot soup in warmed bowl, top with cheese, a dollop of crème fraiche, and the crisp bacon. Sprinkle with chopped chives. Enjoy!

Save the Date: 9th Annual Stowe Weekend of Hope

A retreat for cancer survivors and their loved ones. May 1- 3, 2009.

Visit www.stowehope.org

