

'Statins' for cancer could prevent many breast cancers

- 22:00 22 June 2011 by [Andy Coghlan](#)
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Exemestane, a drug already used to treat breast cancer, can more than halve the chances of healthy, post-menopausal women getting the disease in the first place. So concludes a three-year study in 4560 women in the US and Europe.

Only 11 breast cancers arose in women taking the drug, compared with 32 in those given a placebo, a 65 per cent reduction in risk. Crucially, there were no reports of serious side effects such as other cancers or heart disease in the treated women.

Although researchers [demonstrated in the 1990s](#) that the breast cancer drugs tamoxifen and raloxifene also prevent, as well as cure, breast cancers, women have avoided taking them prophylactically because of rare, life-threatening side effects including cancer of the womb lining and heart attacks caused by blood clots.

The team reporting the new results say that the lack of side effects with exemestane could make it far more attractive [as a preventative treatment](#).

Strong and safe

"Our hope is that our trial results turn up the volume on the debate around breast cancer prevention," says [Paul Goss](#) of the Massachusetts General Hospital Cancer Center in Boston, head of the research team.

"Exemestane is substantially more effective than the other drugs against early breast cancer, and our data suggest it is better at protection too," says Goss. "It is also very safe, and that makes it more appealing."

The results were so impressive that at the end of the trial, all the participants were offered ongoing treatment with the drug.

Goss says that women might do well to take the drug for five years or so when they reach menopause, an age when the risk of breast cancer rises because of increases in the hormone oestrogen. The trial results suggest that over three years, for every 94 women taking exemestane, a single case of breast cancer would be prevented.

"Probably thousands or tens of thousands of women [worldwide] could avoid death from breast cancer by using effective risk reduction in the same way that men and women have reduced their risk of heart disease by reducing high blood pressure or cholesterol levels by taking statins," says Goss.

Source blocked

Side effects may be fewer because of the mechanism by which the drug works. All three major preventive breast cancer drugs work by reducing the body's exposure to oestrogen, but whereas tamoxifen and raloxifene compete with oestrogen for receptors on breast and other

cells, exemestane suppresses production of oestrogen by neutralising aromatase, the enzyme that makes it.

[Enthusiasts for preventive therapy](#) have hailed the results in an editorial accompanying the study in the *New England Journal of Medicine*, concluding that with breast cancer the second most common fatal cancer in the US, "we have run out of excuses... What are we waiting for?"

"We have studied this area of breast cancer risk reduction intensively, and it's now time to put the results of our clinical trials into practice," says [Nancy Davidson](#) of the University of Pittsburgh Cancer Institute in Pennsylvania, a co-author of the editorial.

"About 200,000 women are diagnosed with breast cancer each year, and about 40,000 die," she told *New Scientist*. "Exemestane offers women and physicians another choice in addition to tamoxifen and raloxifene, so having multiple options is good,"

Goss says that another attraction is that the cost of exemestane – currently \$600 per year – is falling dramatically around the world because the patents for it are running out, allowing cheap versions to be made and sold instead.

[Pete Sasieni](#) of the Wolfson Institute of Preventive Medicine in London says the results are "very encouraging", and may persuade some women to consider taking the drugs. But the big question is whether taking them for a short time, say five years beginning at 55, will then have a lifelong protective effect, as has been seen with tamoxifen.

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Aromatase Inhibitors benefit and side effects, toxicity, caution, danger, review of studies by [Ray Sahelian, M.D.](#) Alternatives, supplements and herbal extracts
Aromatase, an enzyme of the cytochrome P450 family, is a very important pharmacological target, particularly for the treatment of breast cancer.

In premenopausal women ovaries are the major sites of [estrogen](#) production, while in postmenopausal women estrogen is produced by aromatization of ovarian and adrenal [androgens](#) in extragonadal sites, mostly in adipose tissue. Aromatase is a cytochrome P450 hemoprotein-containing enzyme complex that catalyzes the rate-limiting step in the conversion of androstenedione and testosterone to estrone and estradiol (E2). Aromatase inhibitors (AIs) have been developed primarily for use in either natural or surgical postmenopausal patients. In premenopausal women, the ovary can overcome the estrogen blockade by reflex increments of luteinizing hormone (LH) and follicle stimulating hormone (FSH), so AIs must be combined with a gonadotropin releasing hormone (GnRH) agonist to prevent the reflex LH and FSH increments.

Natural aromatase inhibitors, how effective are they?

Natural aromatase inhibitors include flavones, flavanones, resveratrol, oleuropein and others. Some of these can be purchased online such as chrysin, genistein, and quercetin.

I have question regarding natural aromatase inhibitors (natural supplements).
Have there been reliable human studies regarding natural aromatase inhibitors?
Are there natural alternatives to Tamoxifen and Lupron?

Plants have substances that have potential aromatase inhibiting activity. Some of

these include flavonoids, for instance quercetin, [chrysin](#), naringenin, apigenin, and Genistein. Not enough human research is available to determine which of the flavonoids or other substances found in plants are the most effective aromatase inhibitors. As a general rule, it is preferable to ingest a variety of flavonoids rather than focusing on only one or two although it is possible that in the treatment of a particular medical condition a specific natural aromatase inhibitor may be more effective.

Are natural aromatase inhibitors useful in breast cancer prevention or post breast cancer treatment?

This is a good question. I suspect that certain natural substances could potentially be helpful in reducing the incidence of breast cancer or as a post breast cancer surgery treatment, but I have not seen specific human studies that have tested natural aromatase inhibiting supplements.

Do you have aromatase inhibitors such as quercetin, chrysin, naringenin, apigenin, and genistein? Also what foods act as aromatase inhibitors to stop estrogen for women?

See the link above for chrysin. Quercetin and genistein are sold as supplements. As to foods, it is difficult to say since most foods have quite a number of different compounds and substances in them and it would be difficult to pinpoint a particular food as having specific aromatase inhibiting activity.

Among all natural products manufactured, have you got any "anti aromatase" product. You know better than me that sometimes testosterone or DHEA might be converted into estrogens.

Aromatase inhibitor drugs

The aromatase enzyme catalyses the last step in estrogen biosynthesis. There are two classes of third-generation aromatase inhibitors: irreversible steroidal inhibitors (e.g. exemestane) and reversible non-steroidal inhibitors (e.g. anastrozole, letrozole). All three agents have been found to be equivalent or superior to megestrol acetate as second-line therapy for metastatic breast cancer.

Aromatase inhibitors include anastrozole, made by AstraZeneca Plc under the brand name Arimidex, and exemestane, made by Pfizer Inc. under the brand name Aromasin.

Aromatase inhibitor drugs and bone loss

Breast and prostate cancer treatment can lead to bone loss and increase the risk for osteoporosis and fractures. Fred Saad, M.D., Université de Montréal's Faculty of Medicine and the Centre Hospitalier de l'Université de Montréal (CHUM), Montreal, Quebec, and colleagues evaluated data from more than 3,500 breast and prostate cancer studies. They found that breast cancer patients treated with aromatase inhibitors were more likely to have bone loss and fractures compared with patients who didn't receive the drug therapy. Similarly, men who received androgen deprivation therapy to treat their prostate cancer had an increased risk of bone disorders. Although the numbers vary from one study to the next (from 5%-45%), an elevated risk is consistently observed. Ways to combat the bone loss, such as exercise, and vitamin D intake may be beneficial.

Aromatase Inhibitors and Breast Cancer

The widespread use of tamoxifen has led to improvements in survival for postmenopausal women with early-stage hormone receptor-positive breast cancer; however, approximately 30% of patients die despite receiving tamoxifen as adjuvant treatment. In addition, concerns exist regarding tamoxifen-associated side effects, including endometrial cancer and thromboembolic disease. The development of the third-generation aromatase inhibitors (AIs; [anastrozole](#), exemestane, and letrozole) therefore represents a potential alternative to tamoxifen.

Women with breast cancer who switch from tamoxifen to a newer class of drugs called aromatase inhibitors live longer. Dr. Lauren Cassell of Lenox Hill Hospital in New York said the research is changing how doctors treat breast cancer patients after their tumors are surgically removed. "If they have been on tamoxifen we are switching them to an aromatase inhibitor. If they are newly diagnosed we are using an aromatase inhibitor instead of tamoxifen," she said in a statement. But tamoxifen remains the main option for younger women with breast cancer. "Aromatase inhibitors are only for women who are post-menopausal," Dr. Lauren Cassell said. Dr. Francesco Boccardo of the National Cancer Research Institute and the University of Genoa in Italy and colleagues looked at two studies of 828 women. About half the women got tamoxifen for five years, as was once recommended, and half got tamoxifen at first and then switched to an aromatase inhibitor after two or three years. The women who switched were much less likely to die of breast cancer or of anything else, Dr. Francesco Boccardo reported.

Endometriosis

Aromatase inhibitors may be helpful in treating [endometriosis](#).

Aromatase Inhibitors and estrogen cream

By increasing levels of estrogen in the body, use of vaginal estrogen products may counter the effects of aromatase inhibitors and thereby raise the risk of breast cancer recurrence. Roughly a fifth of women who use aromatase inhibitors have vaginitis resulting from a lack of estrogen. While estrogen replacement therapy could, in theory, help aromatase inhibitor users with this condition, it is not recommended due to its ability to raise levels of estrogen in the body. Therefore, vaginal estradiol products are often used. However, there is a potential of significant increase in serum estradiol levels after starting vaginal estradiol therapy.

Heart disease risk

Postmenopausal women with early breast cancer who take aromatase inhibitors are more likely to develop heart disease than those who take the old standby tamoxifen, San Antonio Breast Cancer Symposium, San Antonio, Dec. 8-12, 2010. Eitan Amir, MD, senior fellow, oncology and hematology, Princess Margaret Hospital, Toronto. Aman Buzdar, MD, department of breast medical oncology, University of Texas M.D. Anderson Cancer Center, Houston.

Precocious puberty

Aromatase inhibitors have been used in the treatment of selective forms of precocious puberty since the mid-1980s. The primary aim of therapy is attenuation of the effects of estrogen on growth, skeletal maturation, and secondary sexual development. The first-generation agent, testolactone, has been demonstrated to be tolerable and effective in the treatment of familial male precocious puberty,

while mixed results with testolactone have been achieved in girls with McCune-Albright syndrome.

Aromatase inhibitor side effect of thinning bones

The bones of breast cancer patients age prematurely as a result of chemotherapy and aromatase inhibitor therapy. Tamoxifen drug is bone-sparing while aromatase inhibitors cause **bone** loss." Examples of aromatase inhibitors include anastrozole, sold as Arimidex, and exemestane sold as Aromasin.

Toxicity, caution, danger, adverse events

The aromatase inhibitors are increasingly used as adjuvant therapy in postmenopausal women with hormone receptor positive breast cancer. The symptomatic side effects of aromatase inhibitors include: hot flashes, arthralgias, vaginal dryness, mood changes and dyspareunia. The mechanism of arthralgias is uncertain and anti-inflammatory agents are seldom effective. Patients who experience severe musculoskeletal discomfort may necessitate switching to another endocrine agent such as tamoxifen. Physicians should be aware of 'silent' side effects. Screening for bone loss and hypercholesterolemia is critical and patients should be treated accordingly.

Aromatase inhibitors and bipolar mood disorder: a case report.

Bipolar Disord. 2006. Goodwin GM. University Department of Psychiatry, Warneford Hospital, Headington, Oxford, UK.

The aromatase inhibitor letrozole produced irritable mood elevation followed by depression in a woman with a history of postpartum depression. A 60-year-old Caucasian woman who had a severe depressive episode after the birth of her only child, 32 years earlier, was treated successively with anastrozole and letrozole following a mastectomy, radiotherapy and chemotherapy. The patient was prescribed anastrozole for about 6 weeks. During this time she experienced labile mood, increased activity, tremulousness and difficulty sleeping. These symptoms disappeared after stopping the anastrozole. On letrozole, she developed an acute irritable activated mood elevation, which then subsided into a prolonged major depression after withdrawal of letrozole. These effects occurred during co-prescription of amitriptyline at a low dose for urinary frequency. The present case suggests caution may be warranted when employing aromatase inhibitors, especially in women with a past history of postpartum affective disorder or bipolar disorder. As with postpartum mania, the primary mechanism of the effect may be acute reduction in circulating estrogen levels.

The heart disease risk associated with adjuvant aromatase inhibitor treatment is increased compared with tamoxifen therapy in postmenopausal women with early breast cancer. Aromatase inhibitors are superior to tamoxifen in the setting of metastatic breast cancer, but increased cardiac events are associated with their use. Cancer 2008.

questions

Q. I was looking at purchasing quercetin supplement. I've read that quercetin is one of the best flavones and aromatase inhibitors, however you don't mention that it's an aromatase inhibitor on your webpage. Is quercetin also an aromatase inhibitor? Is quercetin safe for women? Which supplements can also be considered aromatase inhibitors?

A. Plants have substances such as flavonoids that influence or inhibit the aromatase enzyme. There are countless substances in plants that inhibit aromatase, not just quercetin. Some of these include chrysin, naringenin, apigenin, and genistein. Not enough research is available to determine which of the flavonoids or other substances found in plants is the most effective aromatase inhibitor. As a general rule, it is preferable to ingest a variety of flavonoids rather than focusing on only one or two.

Q. I am purchasing chamomile, Olive-Leaf-Extract, and quercetin. I think these are aromatase inhibitors and I do want suppress decrease my estrogen levels because I have endometriosis, however, I'm wondering if taking one of each 5 days a week considered "too much"?

A. We can't make that decision for you. Please discuss with your personal health care consultant. What may be too little for one person may be too much for another and we have no way of knowing your full medical history, lab studies, and physical exam results.

I would like to thank you for providing such an extremely informative website. It has been very helpful for me in treating health issues naturally. I was diagnosed several months ago with low testosterone and slightly high estrogen. I'm on a quest to increase testosterone and DHT levels in my body, and reduce estrogen levels. Besides my daily liquid basic multivitamin, I am taking 900 mg of gamma oryzanol daily to boost testosterone levels, and this does help. I was wondering if there are any natural supplements that will inhibit aromatase without inhibiting 5 alpha reductase also. I know mushrooms can inhibit aromatase, but i've read that mushrooms also inhibit dht also. Can I inhibit aromatase without lowering DHT? Thank you for your help with this matter.

There are several herbs that have an influence on these enzymes, but they are not as specific as pharmaceutical medications. Rather than focusing to such detail on which enzymes or chemicals in the body to alter, I prefer to focus on the overall health of the body and treat overt signs and symptoms rather than treat laboratory numbers from blood studies.

Does anyone know of a topical herbal hair product for menopausal female with hair loss and high levels of serum DHT? If not, any leads on what herbs or otherwise one might use to make something topical? Any research or anecdotal evidence to support? Also, do you think long acting T3 vs. T4 supplementation works the same on the conversion of testosterone to DHT?

I am not aware of a natural herbal product used topically that has been proven to work for hair loss although there are some companies working on such products and there may be one soon. I have not seen any research on the difference between long acting T3 versus T4 in terms of influence on the conversion of testosterone to DHT.

5-alpha reductase Inhibitors

[Propecia](#) and Proscar are the brand names for finasteride.

Aromatase in Estrogen Biosynthesis

The conversion of androgens to estrogens by aromatase is the last step in one of the three major steroidogenic pathways (Figure 1).^[75,76] The aromatase-enzyme complex consists of a specific

cytochrome P450 (CYP) heme protein in conjunction with a fluoroprotein, CYP reductase.[77] Localized primarily to the endoplasmic reticulum of ovarian granulosa cells in premenopausal women, the enzyme also is expressed in a variety of tissues including liver, brain, and testes. [78-81] Biologically significant aromatase activity in adipose tissue is the principal source of estrogens after menopause.[82,83] Although synthesis of ovarian aromatase is regulated by an ovarian-pituitary (e.g., estro-gen-follicle-stimulating hormone) feedback loop, a similar mechanism including specific stimulants or inhibitors of aromatase expression in adipose tissue has not been confirmed (Figure 2).[84]

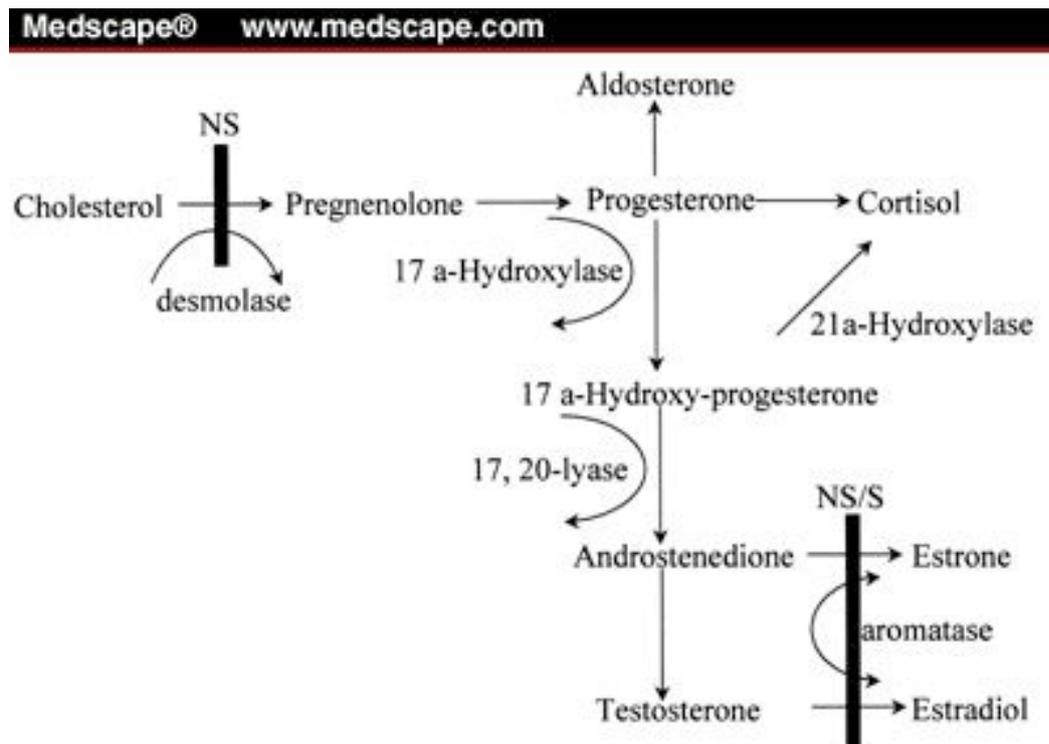


Figure 1.

Effect of aromatase inhibitors on steroidogenesis. Primary sites of selective (S) and nonselective (NS) blockade are indicated by heavy bars. S = new aromatase inhibitors; NS = aminoglutethimide.

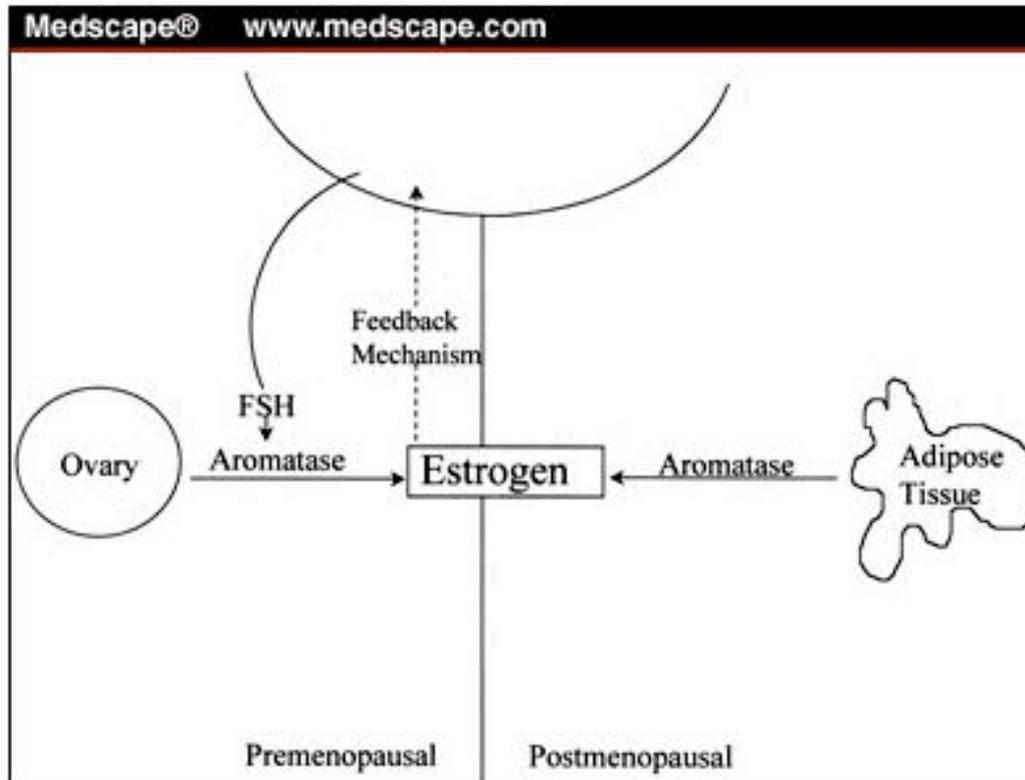


Figure 2.

Primary sources of estrogen biosynthesis in women. Aromatase inhibitors suppress (ovarian and peripheral (e.g., adipose tissue) estrogen production. Suppression of plasma estrogen concentrations cannot be maintained in premenopausal women because of the endocrine feedback loop, which induces a stimulating hormone.

Primary sources of estrogen biosynthesis in women. Aromatase inhibitors suppress ovarian and peripheral (e.g., adipose tissue) estrogen production. Suppression of plasma estrogen concentrations cannot be maintained in premenopausal women because of the endocrine feedback loop, which induces aromatase activity. FSH = follicle-stimulating hormone.

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Exemestane Side Effects

Brand Names: *Aromasin*

Please note - some side effects for Exemestane may not be reported. Always consult your doctor or healthcare specialist for medical advice. You may also report side effects to the FDA at <http://www.fda.gov/medwatch/> or 1-800-FDA-1088 (1-800-332-1088).

Side Effects of Exemestane - for the Consumer

Exemestane

All medicines may cause side effects, but many people have no, or minor, side effects. Check with your doctor if any of these most COMMON side effects persist or become bothersome when using Exemestane:

Anxiety; back, joint, muscle, or limb pain; constipation; coughing; diarrhea; dizziness; flu-like symptoms; hair loss; headache; hot flashes; increased or decreased appetite; increased sweating; nausea; stomach pain or upset; tiredness; trouble sleeping; weight gain; vomiting.

Seek medical attention right away if any of these SEVERE side effects occur when using Exemestane:

Severe allergic reactions (rash; hives; itching; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue); chest pain; confusion; depression; fainting; general feeling of being unwell; numbness, burning, or tingling in the skin, hands, or feet; numbness of an arm or leg; one-sided weakness; severe or sudden bone pain; severe stomach pain; shortness of breath; sudden, severe dizziness, headache, or vomiting; sudden, unusual weight gain; swelling of the hands, legs, or feet; vision or speech changes; yellowing of the skin or eyes.

This is not a complete list of all side effects that may occur. If you have questions about side effects, contact your health care provider. Call your doctor for medical advice about side effects. To report side effects to the appropriate agency, please read the [Guide to Reporting Problems to FDA](#).

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Side Effects by Body System - for Healthcare Professionals

Musculoskeletal

Musculoskeletal side effects including arthralgia (14.6% to 28.8%), pain in limb (9%),

osteoarthritis (5.9%), myalgia (5.5%), back pain, pathological fracture, and skeletal pain have been reported. Reductions in bone mineral density over time have also been reported.

General

General side effects including fatigue (11% to 22%), hot flushes (13% to 32.9%), pain (13%), edema (5.5% to 7%), influenza like symptoms (6%), asthenia (6%), and fever (5%) have been reported.

Immunologic

Immunologic side effects including grade 3 or 4 lymphocytopenia (20% of patients in clinical trials for advanced breast cancer) and infection have been reported.

Of the advanced breast cancer patients with grade 3 or 4 lymphocytopenia, 89% had a preexisting lower grade lymphopenia. Forty percent of patients either recovered or improved to a lesser severity while on treatment.

Gastrointestinal

Gastrointestinal side effects including nausea (8.5% to 18%), dyspepsia (16%), abdominal pain (6% to 11%), diarrhea (4% to 9.6%), vomiting (7%), anorexia (6%), constipation (5%), and increased appetite (3%) have been reported.

Dermatologic

Dermatologic side effects including increased sweating (11.8% to 17.8%), alopecia (15.1%), dermatitis (8.2%), hypoesthesia, rash, and itching have been reported.

Cardiovascular

Cardiovascular side effects including hypertension (5% to 15.1%) and chest pain have been reported.

Hepatic

In the comparative study in advanced breast cancer patients, CTC grade 3 or 4 elevation of gamma glutamyl transferase without documented evidence of liver metastasis was reported in 2.7% of patients treated with exemestane and in 1.8% of patients treated with megestrol acetate.

Hepatic side effects including elevations of serum levels of AST, ALT, alkaline phosphatase, and gamma glutamyl transferase greater than five times the upper value of the normal range have rarely been reported in patients treated for advanced breast cancer (but appear mostly attributable to the underlying presence of liver and/or bone metastases).

In early breast cancer patients, elevations in bilirubin, alkaline phosphatase, and creatinine were more common in those receiving exemestane than either tamoxifen or placebo. Alkaline phosphatase elevations of any CTC grade (13.7% to 15.0%), treatment emergent bilirubin elevations (any CTC grade) (5.3% to 6.9%), CTC grade 3 to 4 increases in bilirubin (0.9%), and creatinine elevations (5.5% to 5.8%) have been reported.

Cholestatic hepatitis has been reported during postmarketing surveillance.

Psychiatric

Psychiatric side effects including insomnia (12.4% to 13.7%), depression (6.2% to 9.6%), and anxiety (4.1%) have been reported.

Nervous system

Nervous system side effects including headache (6.9% to 13.1%), depression (13%), insomnia (11%), anxiety (10%), dizziness (8% to 9.7%), confusion, and paresthesia have been reported.

Respiratory

Respiratory side effects including dyspnea (10%), coughing (6%), upper respiratory tract infection, pharyngitis, rhinitis, bronchitis, and sinusitis have been reported.

Local

Local side effects including pain at tumor sites (8%) have been reported.

Ocular

Ocular side effects including visual disturbances (5%) have been reported.

Oncologic

Oncologic side effects reported from animal studies have included an increased incidence of hepatocellular adenomas and/or carcinomas as well as an increased incidence of renal tubular adenomas. Exemestane has also been clastogenic in human lymphocytes in vitro without metabolic activation.

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Article

Emerging Data on Side Effects of Aromatase Inhibitors

Goodman, Alice

[Free Access](#)

SAN ANTONIO-Aromatase inhibitors (AIs) are gaining favor over tamoxifen for the treatment of postmenopausal hormone receptor-positive breast cancer. Originally AIs were thought to improve upon the side-effects profile of tamoxifen, and although they are free of

some of the side effects, longer experience using AIs has brought to light different side effects.

Several poster studies at the San Antonio Breast Cancer Symposium focused on side effects such as arthralgias and myalgias, sexual and gynecologic side effects, and potential retinal problems-some of which can lead to poor adherence to treatment.

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Adherence

Even though there is a strong evidence base supporting the use of AIs in postmenopausal, estrogen receptor (ER)-positive breast cancer, a substantial proportion of women treated in academic clinical practices have discontinued this therapy because of toxicity, noted Susan Dent, MD, a medical oncologist and Head of Clinical Trials at Ottawa Hospital Regional Cancer Centre.

The discontinuation rates of AI therapy that we found in this study of women with early breast cancer are of great concern, Dr. Dent said. The results suggest that interventions are needed to enhance compliance in women taking an AI. She suggested that doctors and nurses discuss potential side effects of AIs prior to treatment, and recommended nonsteroidal inflammatory drugs for musculoskeletal pains.

The study was based on a retrospective chart review of 640 postmenopausal women with early-stage hormone-sensitive breast cancer who were treated with an AI at the Ottawa Hospital Regional Cancer Centre between January 1, 1999 and December 31, 2006.

Figure. Susan Dent, ...

[Image Tools](#)

The women received an AI either as upfront therapy for five years (43%), as part of a switching strategy after two to three years of tamoxifen (36%), or as extended therapy after five years of tamoxifen (21%). The average age at diagnosis was 60.3.

Stage I patients represented 32% of the study population; Stage IIa, 36%; Stage IIb, 19%; Stage IIIa, 7%; and Stage IIIb, 7%. Seventy-eight percent of patients were both ER and progesterone receptor (PR) positive; and 17% were ER-positive and PR-negative.

Toxicity was reported by 42% of patients, and AI therapy was stopped due to toxicity in 19%. The toxicities reported were similar to those reported elsewhere, except that fewer hot flashes were reported. Osteoporosis was found in a higher proportion of patients on an aromatase inhibitor than has been reported in the literature, but 17% of patients had documented bone loss prior to therapy.

Myalgias/arthralgias were the most commonly reported toxicities, occurring in 30% of patients (197 of 640), of whom about 21% (42) discontinued AI therapy. Self-reported fracture rates were low in this study (4%) and did not appear to increase with longer duration of therapy.

Dr. Dent said that withdrawal rates due to toxicity were higher in this study than in the big studies reported in the literature: ATAC, 11.1%; IES, 4.5%; and 4.5% in MA-17. In our experience, women were more likely to stop an AI within the first two years of therapy [32%],

she said.

In this study, no differences in toxicities were seen based on choice of AI, she added. Also, receptor status, age, and HER-2 status did not influence discontinuation rates of AI therapy, but patients who had prior systemic chemotherapy were more likely to stay on AI therapy (16.3% discontinued) than those who did not receive prior chemotherapy (21.8% discontinued), although this difference was not statistically significant.

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Aches, Pains

Musculoskeletal pains are problematic for about 5% to 10% of women on aromatase inhibitors, said Kathleen Pritchard, MD, Senior Scientist and Chair of the Breast Group at Sunnybrook Odette Cancer Center in Toronto. These side effects definitely reduce compliance.

Although both tamoxifen and AIs are much more tolerable than chemotherapy, they are hormones and have hormonal effects. All drugs, including hormonal agents, cut two ways—having both risks and benefits, she said.

Dr. Pritchard said that in her practice, when a woman who is taking an adjuvant AI finds the myalgias and arthralgias difficult to tolerate, Dr. Pritchard will switch to another AI.

However, my impression is that all AIs can cause muscle aches and pains, she commented. If no AI can be tolerated, I will definitely switch to tamoxifen if the patient has not already completed five years of it, or with the new ATLAS data [also reported at the San Antonio meeting, suggesting that tamoxifen has benefits that extend beyond five years], perhaps even then. In the adjuvant setting, I would rather have my patients taking some hormonal agent than nothing. And tamoxifen is still an effective drug.

Another problem related to adherence to AIs is that there is no feedback loop to show patients that the drugs are effective. With statins or antihypertensive agents, cholesterol levels and blood pressure lowering effects can be measured, giving patients the reassurance that these drugs are working. However, with drugs for cancer prevention, you are treating in a vacuum.

Adherence would be improved if measurements could reflect the benefits of the drugs, Dr. Pritchard continued. She said that oncologists and nurses should reinforce the benefits of hormonal therapy, explaining to patients that these drugs cut the risk of recurrence by 50% from 2% a year for node-negative patients and 4% a year for node-positive patients. If they know they are cutting the risk in half, they will probably feel the drugs are worth taking even with the side effects, she said.

Figure. Kathleen Pri...

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Long-Term Effects

Despite the therapeutic benefit of exemestane observed in the original Intergroup Exemestane

Study, a cohort of 582 women randomized to exemestane and tamoxifen had persistent sexual and gynecologic effects at seven years of follow-up-mainly, dyspareunia and loss of libido, according to data presented by Lesley J. Fallowfield, MD, Director of the CRUK Sussex Psychosocial Oncology Group at Brighton & Sussex Medical School.

All women included in the study were treated with tamoxifen for two to three years and then randomized to continue on tamoxifen or to switch to exemestane for another two to three years; they all completed five years of hormonal therapy and then were followed for an additional two years.

Overall quality of life did not differ between the two groups at any time point, Dr. Fallowfield said. The efficacy of exemestane was not at the expense of quality of life in general. However, individual symptoms are troublesome and persistent-for example, vaginal bleeding and discharge on tamoxifen and vaginal dryness, dyspareunia, and loss of libido on exemestane. Libido never recovered when off treatment.

Severe loss of libido was reported in about one third of each group seven years after starting on tamoxifen. Loss of libido is a side effect of all hormonal therapy, Dr. Fallowfield noted. But you can ameliorate this problem by giving women who start on this type of therapy education about what to expect and practical advice about the need for lubrication.

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Overlooked Problem

Dr. Pritchard added that the problem of sexual side effects is often overlooked but it is a big issue for some women. She said that devices like the Estring, which provides slow, continuous, local delivery of estrogen, or intra-vaginal estrogen cream used sparingly can be helpful for vaginal dryness, but this remains controversial for breast cancer survivors.

In the MA-17 trial, she said, intra-vaginal estrogen cream was allowed for symptoms of vaginal dryness. We are now reviewing the use, and hope, if numbers allow, to analyze whether any effect on efficacy was seen.

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Retinal Hemorrhages

A small percentage of women taking anastrozole for early breast cancer experience small retinal hemorrhages, according to a retrospective study reported by Alvin Eisner, PhD, Senior Scientist at the Neurological Sciences Institute and Research Associate Professor at the Casey Eye Institute, both of Oregon Health & Science University.

Although the clinical significance of these hemorrhages is not known, Dr. Eisner recommended that women taking hormonal therapy for breast cancer who experience visual changes should undergo optical coherence tomography (OCT), a powerful, new, non-invasive technology that is readily available, and have their vision monitored at periodic intervals.

Figure. Regarding th...

[Image Tools](#)

The study included 35 anastrozole users, 38 amenorrheic tamoxifen users, and 53 amenorrheic controls who were not using hormone replacement. Conventional retinal fundus photography of both eyes of each subject taking hormonal therapy and of controls were evaluated for the presence of retinal hemorrhages by an ophthalmologist without knowledge of the subjects' information.

Photographs from an additional 36 women taking tamoxifen who were recruited for a previous study were also assessed for hemorrhages.

OCT was used to measure retinal thickness and to detect posterior vitreous detachments (PVD). At the time of the San Antonio meeting, OCT was analyzed for one eye in each subject in: 17 non-PVD anastrozole users, 18 non-PVD tamoxifen users, and 23 non-PVD controls.

Retinal hemorrhages were found in four users of anastrozole, one user of tamoxifen, and none of the control patients.

Dr. Eisner said that the OCT scans suggest that anastrozole users often are subject to a pronounced degree of vitreo-retinal traction that results from estrogen depletion and may sometimes lead to retinal hemorrhages.

Other factors, such as the use of aspirin and bisphosphonates for controlling common anastrozole-induced side effects, may also contribute to the development of retinal hemorrhages, he suggested. Further study of the ocular and visual effects of AIs is warranted, he said.

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ASCO's Choices for Top Cancer Advances of 2007

On the American Society of Clinical Oncology's annual list of the most significant advances in cancer treatment, prevention, and screening for last year, as chosen by a 21-member oncologist editorial board, were the following (listed in no particular order, a news release notes):

- The first systemic treatment for primary liver cancer.
- Treatments for advanced kidney cancer continue to expand.
- MRI better for screening women at high risk for breast cancer.
- HPV linked to head and neck cancers; possible new role for HPV vaccine.
- Drop in breast cancer linked to declining use of hormone-replacement therapy.
- Preventive radiation therapy can stop the spread of advanced lung cancer.