Soy Foods, Diet, and Tamoxifen

Oncology Nutrition
a dietetic practice group of the Academy of Nutrition and Dietetics

Question:

Are there any foods I should avoid while taking tamoxifen? What about soy foods and flaxseeds?

Answer:

What is tamoxifen?

Tamoxifen is a medication known as a selective estrogen receptor modulator, or SERM. Tamoxifen often is prescribed as part of the treatment for ER+ breast cancer. Tamoxifen binds with estrogen receptors, without activating growth, in breast cancer cells. In this way, *tamoxifen prevents cancer cells from binding to a women's own estrogen*. As a result, breast cancer cell growth is blocked.

Why is there concern over food and tamoxifen?

It is smart to have concerns about things that you eat, or take, such as dietary supplements, that may lessen the effectiveness of your medications. Tamoxifen is no different. You certainly don't want to take a medication to reduce breast cancer risk, only to eat or drink something that renders the tamoxifen less effective.

The food of most concern for women taking tamoxifen is grapefruit. Grapefruit is well-known to interfere with numerous medications. Many drug-interaction resources specifically advise that women taking tamoxifen avoid grapefruit. For this reason, you shouldn't drink grapefruit juice or regularly eat whole grapefruit if you are taking tamoxifen or other medications to reduce your breast cancer risk.

While there are no other foods known to have an interaction with Tamoxifen or affect its absorption, there are some foods that get more attention when it comes to breast cancer and survival, and may even work with anti-cancer medications. Some of those foods are discussed below.

Soy

Soybeans are a species of legume and are used to make soy milk and tofu. Fermented soy foods include fermented soy bean paste, natto, and tempeh. Soybeans are good sources of protein, Vitamin C, folate, and fiber. Confusion about the health effects of soy foods arises from the term "phytoestrogens." The "phytoestrogen" nutrients in soy are called isoflavones. The isoflavones have

chemical structures that look a bit like the estrogen found in a woman's body. This is where the term phytoestrogen originated. However, phytoestrogens are not the same thing as female estrogens. ***Soy foods do not contain estrogen***.

Because of the concern around the "phytoestrogens" in soy foods, some people have recommended that women taking tamoxifen should avoid soy foods, because these foods might "undo" the estrogen blocking effects of the medication. Ongoing research supports the opposite conclusion—soy foods appear to *enhance* or improve the breast cancer blocking actions of tamoxifen.

A review of studies published in 2019 which pooled over 330,000 human participants found that soy protein intake was associated with a decreased risk in the mortality of breast cancer. The current findings support recommendations to increase intake of soy for greater longevity.

Extensive clinical and epidemiologic data show that isoflavone intake does not adversely affect markers of breast cancer risk (such as mammogram results). Studies involving over 11,000 women from the USA and China show that soy intake statistically reduces recurrence and improves survival in breast cancer patients. Evidence suggests that soy consumption during childhood and/or adolescence can help to reduce breast cancer risk. Post diagnosis soy intake can reduce recurrence and improve survival.

Cell and animal studies have shown that adding soy food nutrients to tamoxifen inhibits the growth of estrogen receptor positive (ER+) breast cancer cells. Even more encouraging are numerous studies showing that women who regularly eat soy foods have a lower risk of breast cancer and breast cancer recurrence. This is true for both Asian and American women, for women who ate soy foods early in life and for women who added them into their diet as adults. One study from Korea found that even for women who had a BRCA 1 or 2 mutation, eating soy foods appears to reduce the risk of breast cancer.

One research review considered a total of 131 articles, including 40 randomized controlled trials, 11 uncontrolled trials, and 80 observational studies. This study supports soy's safety for women with a history of breast cancer, noting "*Soy consumption may be associated with reduced risk of breast cancer incidence, recurrence, and mortality. Soy does not have estrogenic effects in humans. Soy intake consistent with a traditional Japanese diet appears safe for breast cancer survivors*." In most of these studies, a significant proportion of the study participants were taking tamoxifen.

If you would like to eat soy foods, it appears that this is safe, and potentially beneficial. One to two servings of soy foods daily is a good amount. A serving could be ½ cup edamame, 8oz of soy milk or 4oz of tofu. However, if you don't enjoy soy foods, there is no reason that you have to eat them. If soy is not for you, focus on other lifestyle interventions, such as exercise for good health. At this time, there isn't enough information about soy supplements, such as concentrated isoflavones, to know if they are safe. You should not take concentrated soy supplements.

Flaxseeds

Flaxseeds are tiny seeds with a hard shell, a bit larger than a sesame seed. They are a good source of healthy fat, antioxidants and fiber but need to be ground up prior to ingestion for maximum benefit. As with soy foods, many women have concerns about flaxseeds, because they too contain nutrients that are referred to as "phytoestrogens." The "phytoestrogen" nutrients in flaxseeds are called lignans.

What we do know suggests that flaxseeds are safe for women taking tamoxifen. Cell, animal and human studies support that flaxseed lignans can significantly decrease the growth of breast cancer cells.

More studies are now available on flaxseeds in women with breast cancer. In one study, researchers looked at cancer cells from breast biopsies of women who were diagnosed with breast cancer. Half of these women were randomly selected to eat muffins containing flaxseeds, while the other half ate a "control" (no flaxseed) muffin. Researchers then were able to collect breast tumor cells again, from the mastectomies and lumpectomies that these women had as part of their treatment. In this way, the researchers could look at how the cancer cells were "behaving" before and after the women ate flaxseeds. Compared with cells from the women eating the control muffins, the breast cancer cells from the women who ate the flaxseeds muffins had a lower rate of tumor cell proliferation (growth) and a higher rate of apoptosis (cancer cell death). Estrogen and progesterone receptor levels on the cancer cells did not change in either group, meaning that the flaxseeds did not affect these receptor levels.

One research review considered 2 randomized controlled trials, 2 uncontrolled trials, 1 biomarker study, and 5 observational studies. This study supports the safety of flaxseeds for women with a history of breast cancer, noting, "*Current evidence suggests that flax may be associated with decreased risk of breast cancer. Flax demonstrates antiproliferative effects in breast tissue of women at risk of breast cancer and may protect against primary breast cancer. Mortality risk may also be reduced among those living with breast cancer*."

In 2013 a large epidemiology study with more than 6,000 women showed flaxseed consumption is associated with a reduction in risk of breast cancer in humans. In this study, women consumed a flaxseed product (such as flax bread) at least twice weekly.

In 2014 a systematic review of flaxseed for potential impact on risk of breast cancer incidence or recurrence in women living with breast cancer showed mostly favorable effects of flaxseeds intake. The authors included 10 studies with over 1,800 human subjects and concluded that flaxseed may be associated with decreased risk of breast cancer.

A literature reviewed found that some clinical trials showed flaxseed can have an important role in decreasing breast cancer risk, mainly in postmenopausal women. The authors felt that further studies are needed, specifically more clinical trials in humans.

As with soy foods, flaxseeds appear to be safe, and potentially beneficial for both women with a history of breast cancer and for prevention. If you would like to eat ground flaxseeds, you should feel good about doing so. Based on studies using these amounts, one to four tablespoons of ground flaxseed per day appears to be safe and potentially protective against breast cancer. However, if you don't enjoy flaxseeds, there are other changes you can make to your diet and lifestyle to improve overall health. At this time, there isn't enough information about flaxseed supplements, such as concentrated lignans, to know if they are safe. You should not take concentrated flax supplements.

The original question and answer were generously donated by Diana Dyer, MS, RD a cancer survivor, registered dietitian, organic garlic farmer, and the author of "A Dietitian's Cancer Story: Information & Inspiration for Recovery & Healing from a 3-time Cancer Survivor.

Question and Answer updated by Laura Kelly, MS, RD, CSO, CDN on behalf of the ON DPG

References:

1. Holmes FA, Liticker JD. Pharmacogenomics of Tamoxifen in a Nutshell—And Who Broke the Nutcracker? *JOP* 2005. 1(4):155-59. Accessed Jan 5, 2014: http://jop.ascopubs.org/content/1/4/155.full
2. Magee PJ, Rowland I. Soy products in the management of breast cancer. *Curr Opin Clin Nutr Metab Care*. 2012;15(6):586-91.
3. Mai Z, Blackburn GL, Zhou JR. Genistein sensitizes inhibitory effect of tamoxifen on the growth of estrogen receptor-positive and HER2-overexpressing human breast cancer cells. *Mol Carcinog*. 2007;46(7):534-42.
4. Mai Z, Blackburn GL, Zhou JR. Soy phytochemicals synergistically enhance the preventive effect of tamoxifen on the growth of estrogen-dependent human breast carcinoma in mice. *Carcinogenesis*. 2007;28(6):1217-23.
5. Ko KP, Kim SW, Ma SH, Park B, Ahn Y, Lee JW, Lee MH, Kang E, Kim LS, Jung Y, Cho YU, Lee B, Lin JH, Park SK. Dietary intake and breast cancer among carriers and noncarriers of BRCA mutations in the Korean Hereditary Breast Cancer Study. *Am J Clin Nutr*. 2013;98(6):1493-501.
6. Chi F, Wu R, Zeng YC, Xing R, Liu Y, Xu ZG. Post-diagnosis soy food intake and breast cancer survival: a meta-analysis of cohort studies. *Asian Pac J Cancer Prev*. 2013;14(4):2407-12.
7. Nechuta SJ, Caan BJ, Chen WY, Lu W, Chen Z, Kwan ML, Flatt SW, Zheng Y, Zheng W, Pierce JP, Shu XO. Soy food intake after diagnosis of breast cancer and survival: an in-depth analysis of combined evidence from cohort studies of US and Chinese women. *Am J Clin Nutr*. 2012;96(1):123-32.
8. Caan BJ, Natarajan L, Parker B, Gold EB, Thomson C, Newman V, Rock CL, Pu M, Al-Delaimy W, Pierce JP. Soy food consumption and breast cancer prognosis. *Cancer Epidemiol Biomarkers Prev*. 2011;20:854-58.

9. Guha N, Kwan ML, Quesenberry CP Jr, Weltzien EK, Castillo AL, Caan BJ. Soy isoflavones and risk of cancer recurrence in a cohort of breast cancer survivors: the Life After Cancer Epidemiology study. *Breast Cancer Res Treat*. 2009;118:395-405.
10. Kang X, Zhang Q, Wang S, Huang X, Jin S. Effect of soy isoflavones on breast cancer recurrence and death for patients receiving adjuvant endocrine therapy. *CMAJ*. 2010;182:1857-62.
11. Dong JY, Qin LQ. Soy isoflavones consumption and risk of breast cancer incidence or recurrence: a meta-analysis of prospective studies. *Breast Cancer Res Treat*. 2011;125:315-23.
12. Fritz H, Seely D, Flower G, Skidmore B, Fernandes R, Vadeboncoeur S, Kennedy D, Cooley K, Wong R, Sagar S, Sabri E, Fergusson D. Soy, red clover, and isoflavones and breast cancer: a systematic review. *PLoS One*. 2013;8(11):e81968.
13. Saggar JK, Chen J, Corey P, Thompson LU. Dietary flaxseed lignan or oil combined with tamoxifen treatment affects MCF-7 tumor growth through estrogen receptor- and growth factor-signaling pathways. *Mol Nutr Food Res*. 2010;54(3):415-25.
14. Chen J, Power KA, Mann J, Cheng A, Thompson LU. Flaxseed alone or in combination with tamoxifen inhibits MCF-7 breast tumor growth in ovariectomized athymic mice with high circulating levels of estrogen. *Exp Biol Med (Maywood)*. 2007;232(8):1071-80.
15. Chen J, Hui E, Ip T, Thompson LU. Dietary flaxseed enhances the inhibitory effect of tamoxifen on the growth of estrogen-dependent human breast cancer (mcf-7) in nude mice. *Clin Cancer Res*. 2004;10(22):7703-11.
16. Thompson LU, Chen JM, Li T, Strasser-Weippl K, Goss PE. Dietary flaxseed alters tumor biological markers in postmenopausal breast cancer. *Clin Cancer Res*. 2005;11(10):3828-35.
17. Flower G, Fritz H, Balneaves LG, Verma S, Skidmore B, Fernandes R, Kennedy D, Cooley K, Wong R, Sagar S, Fergusson D, Seely D. Flax and Breast Cancer: A Systematic Review. *Integr Cancer Ther*. 2013 Sep 8.
18. www.aicr.org/foods-that-fight-cancer
19. Nachvak, Seyed Mostafa et al. Soy, Soy Isoflavones, and Protein Intake in Relation to Mortality from All Causes, Cancers, and Cardiovascular Diseases: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies. *Journal of the Academy of Nutrition and Dietetics*, Volume 119, issue 9, 1483-1500. September 2019.
20. Messina M. Impact of soy foods on the development of breast cancer and the prognosis of breast cancer patients. *Forsch Komplementmed.* 2016;23(2):75-80.
21. Lowcoco EC, Cotterchio M, Boucher BA. Consumption of flaxseed, a rich source of lignans, is associated with reduced breast cancer risk. *Cancer Causes Control*. 2013 Apr; 24(4): 816-6.
22. Flower, G, Fritz, H et al Flax and Breast Cancer: A Systematic Review. Integr Cancer Ther. 2014 May;13(3):181-92 Page updated: October 2019