

Antidepressants counteract tamoxifen's recurrence-prevention effects

Tamoxifen is an important medication used to help prevent recurrence of breast cancer. To work in the body, tamoxifen must be changed into a new molecule called endoxifen by an enzyme in the liver. The enzyme, called CYP₄₅₀2D6 is genetically deficient in a minority of women, and these women do not get any benefit from using tamoxifen. Animal studies and laboratory studies in the past have indicated that some antidepressant drugs inhibit the action of this enzyme, even in women who have normal levels. When this enzyme's activity is inhibited, it cannot make endoxifen. The particular antidepressants are the SSRIs or selective serotonin uptake inhibitors (this group includes popular antidepressants such as Paxil and Prozac). Scientists have thought for some time that these antidepressants might actually counteract the recurrence-preventing effects of tamoxifen, and this has recently been confirmed in a study presented at the 2009 American Society of Clinical Oncology meeting.

Scientists searched a database of over 10 million patients to find women who used tamoxifen with or without SSRI antidepressants between 2003 and 2005. The women had to have used tamoxifen regularly for at least two years. They found 945 women who used tamoxifen alone and 353 who used it together with an antidepressant that suppressed CYP₄₅₀2D6. The number of women in the two groups who had breast cancer recurrences was then analyzed. The women taking tamoxifen alone had a 7.5% recurrence rate while the women taking it with antidepressants had a 13.9% recurrence rate – nearly twice the number of recurrences of the tamoxifen-only group. This strongly implicates the SSRI antidepressants as having a negative drug interaction with tamoxifen.

This drug interaction is especially problematic for tamoxifen patients since SSRI drugs have been found to reduce the hot flashes that are often a vexing side effect of tamoxifen, and many women have been prescribed SSRI drugs for this purpose. The new study makes this drug combination quite problematic, and women taking SSRI drugs for their tamoxifen-related hot flashes should contact their physicians to discuss their situation. There are other antidepressants or other types of drugs that may also be effective at reducing hot flashes without this drug interaction. Additionally, the Block Center can also provide a full integrative therapy plan using non-pharmacological as well as appropriate drug therapies to counter side effects of drugs related to cancer treatment, including the depression that accompanies some cancer drugs, without causing negative drug interactions. An example of integrative therapies for hot flashes is acupuncture while depression and other distress can be effectively treated with cognitive-behavioral approaches.

Aubert RE et al. Risk of breast cancer recurrence in women initiating tamoxifen with CYP3D6 inhibitors. Presented at: American Society of Clinical Oncology Annual Meeting, May 30, 2009. *J Clin Oncol.* 27:18s, 2009 (suppl; abstr CRA508).

To summarize: Some types of antidepressant drugs (the selective serotonin reuptake inhibitors or SSRI's) have been implicated in a negative drug interaction with tamoxifen, a medication used to help prevent breast cancer recurrence. These drugs prevent

tamoxifen from being activated in the body. Women taking antidepressants and tamoxifen should consult their doctors about their particular circumstance.