



Happy 4th of July!

PIC QUESTION OF THE WEEK: 6/29/09

Q: Please provide information regarding the potential interaction between tamoxifen and SSRIs.

A: Tamoxifen is a nonsteroidal, selective estrogen receptor modulator (SERM) used since 1977 for the treatment of breast cancer as well preventive therapy for women at high risk of the disease. The drug has been used in both pre- and postmenopausal women. Estrogenic and antiestrogenic activity is dependent on target tissue. The compound antagonizes estrogenic activity in the breast and CNS while serving as an estrogen agonist on bone, endometrium, and lipids. Antiestrogen effects in the CNS appear responsible for the frequent occurrence of vasomotor symptoms (e.g. hot flashes) associated with administration of tamoxifen. Hormone replacement therapy (HRT) is not usually recommended in this population of women. Fortunately, selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) have proven effective for the management of hot flashes in women receiving tamoxifen. These drugs have been shown to reduce the frequency of hot flashes by approximately 60% in comparison to a 25% to 35% decrease with placebo. Venlafaxine, paroxetine, and citalopram have demonstrated the greatest reduction in hot flash frequency while fluoxetine and sertraline have provided only modest improvement. In 2006, an FDA advisory panel recommended that tamoxifen's prescribing information include a statement cautioning that women who were slow CYP2D6 metabolizers might be at increased risk of breast cancer recurrence. This was suggested because the conversion of the parent drug to several active metabolites is dependent on CYP2D6 and other CYP450 isoenzymes. During the past few years, some studies have suggested a potential drug interaction between tamoxifen and the newer generation of antidepressants. This possible interaction, rarely found in drug interaction screening programs, is based on the ability of these agents to inhibit the CYP2D6 isoenzyme, thus reducing conversion of tamoxifen to its active metabolites including 4-hydroxytamoxifen and 4-hydroxy-N-desmethyltamoxifen (endoxifen). Some investigators have cautioned that this interaction may increase the risk of breast cancer recurrence. The relative inhibitory activity of newer antidepressants on CYP2D6 is: ***paroxetine = fluoxetine > duloxetine > fluvoxamine = sertraline = citalopram = escitalopram = venlafaxine.*** Results from recent studies are conflicting. An observational study recently reported at the Annual Meeting of the American Society of Clinical Oncology concluded that strong inhibitors of CYP2D6 (e.g. paroxetine) increased breast cancer rates in women receiving tamoxifen. Another study presented at the same meeting found no association between use of these drugs and the rate of breast cancer recurrence. Although data on this interaction is inconclusive, caution should be taken when prescribing SSRIs, especially the potent inhibitors of CYP2D6, in women receiving tamoxifen.

References:

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