Breast Ca Deaths Up With Paroxetine/Tamoxifen

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VITALS

Major Finding: Risk of breast cancer death was 24%-91% higher when women took paroxetine while on tamoxifen.

Source of Data: Retrospective, population-based cohort study of 2,430 women.

Disclosures: Dr. Kelly reported having no relevant financial disclosures.

SAN ANTONIO — Breast cancer patients who took the antidepressant paroxetine during their course of tamoxifen therapy were up to 91% more likely to die from their disease than were those who did not take the two drugs together, according to a retrospective, population-based cohort study conducted in the Canadian province of Ontario.

Investigators used health card identification numbers to track women aged 66 years and older who were treated with tamoxifen for breast cancer between 1993 and 2005. Almost a third of patients were taking an antidepressant during their tamoxifen therapy, including 2,430 who were taking a selective serotonin reuptake inhibitor.

As a class, SSRIs are known to inhibit cytochrome P450 2D6 (CYP 2D6), an enzyme critical for the conversion of tamoxifen to endoxifen, its active metabolite, in the body. The ability of SSRIs to interfere with the efficacy of tamoxifen—at least in some women—has been theorized, but studies attempting to clarify the issue have reported conflicting results.

In the Canadian study reported at the annual meeting of the San Antonio Breast Cancer Symposium, 1,074 (44.2%) of the women taking an SSRI during tamoxifen therapy had died as of Dec. 31, 2007, when primary data analysis began. After statistical adjustment for age, socioeconomic status, comorbidity, use of other CYP 2D6 drugs, and timing and duration of tamoxifen therapy, investigators found that the breast cancer mortality risk was increased 24% among women who were coprescribed paroxetine during 25% of their tamoxifen treatment.

If patients took paroxetine longer (that is, for more than half of their tamoxifen course), their breast cancer mortality risk rose to 54%. Patients who took both drugs for 75% of the time they received tamoxifen had a 91% risk of breast cancer mortality.

Mortality from any cause was also sharply elevated among women who took paroxetine for 75% or more of their tamoxifen course.

The striking results were significant only for paroxetine, and not for other SSRIs—including fluoxetine, sertraline, fluvoxamine, or citalopram—that were taken concurrently with tamoxifen, reported Dr. Catherine M. Kelly at the meeting.

Dr. Kelly hypothesized that the explanation lies in the degree to which various SSRIs inhibit CYP 2D6. "Paroxetine is the only SSRI that is an irreversible—or 'suicide'—inhibitor of CYP 2D6," she said in an interview.

The dose-response curve of the study, with escalating mortality risk paralleling time on paroxetine, adds significant weight to the findings with regard to paroxetine, marketed as Paxil by GlaxoSmithKline. (The company did not respond to a request for comment on the study.)

Fluoxetine is also a potent inhibitor of CYP 2D6, but was not shown to increase breast cancer mortality in the study. "I would like to see further data on that and would use caution in using any of the drugs that inhibit CYP 2D6 in women who are taking tamoxifen, said Dr. Kelly, who was with the University of Toronto Sunnybrook Health Sciences Centre while conducting the study and is currently a breast medical oncology fellow at the University of Texas M.D. Anderson Cancer Center in Houston.

"There are other options," she noted, including non-SSRI antidepressants that do not inhibit CYP 2D6.

Women need to discuss their choices with a medical oncologist, psychiatrist, or family physician before undergoing tamoxifen therapy, she suggested. ■