Anti-estrogen combo better than single drug for hormone-sensitive breast cancer

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Post-menopausal women with hormone receptor-positive metastatic breast cancer may have a new treatment option that could lengthen their lives, according to results of a study by the SWOG clinical trials network that were presented at the 2011 CTRC-AACR San Antonio Breast Cancer Symposium.

The combination of the two anti-estrogen drugs anastrozole and fulvestrant used in the SWOG S0226 trial extended the median survival time of women with breast cancer by more than six months compared to those who underwent standard treatment with anastrozole alone (47.7 months vs 41.3 months). The combination therapy also lengthened the median time to disease progression (15 months vs 13.5 months).

Lead study coordinator Rita Mehta, M.D., of the University of California, Irvine Medical Center says the results of the phase III trial are particularly exciting because "these patients have not had a new treatment that gave them an overall survival benefit in more than a decade."

Anastrozole (Arimidex®) and fulvestrant (Faslodex®) are both already used in treating breast cancer, though not in combination. The former reduces the production of tumor-promoting estrogen, while the latter interferes with the receptors that allow estrogen to signal cells to grow and reproduce.

Researchers think it's these two different modes of action together that make the combination so effective against hormone receptor-positive breast cancer, the subtype that accounts for more than half of all breast cancers.

"If we take away estrogen and the estrogen receptor, the two together should be better than just doing one at a time," says Mehta.

Starting in the spring of 2004, she and colleagues at 72 other institutions enrolled 707 postmenopausal women with metastatic hormone receptor-positive breast cancer to the trial.

Women were assigned at random to one of the study's two arms. Patients on both arms got a standard 1 mg oral daily dose of anastrozole. Those on the combination arm also got a 250 mg injection of fulvestrant every 28 days, after an initial set of injections to raise the level of fulvestrant in their bloodstream. Researchers saw no significant differences in how well patients tolerated the two therapies.

The overall survival benefit was particularly strong in women who had not previously had tamoxifen therapy for their breast cancer. Among this tamoxifen-naive group (about 60 percent of patients in each arm), median overall survival time on the combination therapy was 47.7 months as compared to 39.7 months for those taking only anastrozole.

The trial researchers are hesitant, however, to focus too much attention on this aspect of the findings. Because plans to analyze the results by prior tamoxifen use were not built into the original trial design, the results of that analysis must clear a higher bar to be found statistically significant.

"We need to better understand other possible factors, since the prior tamoxifen factor could be a false lead from an unplanned analysis," says Mehta, who is eager to see whether even more patients might benefit from this combination treatment.

"The next step for researchers," she says, "would be to try the combination in even earlier stages of breast cancer to test whether long-term cures could be increased at those stages."

More information: Mehta RS, Barlow WE, Albain KS, et al. "A Phase III randomized trial of anastrozole versus anastrozole and fulvestrant as

first-line therapy for postmenopausal women with metastatic breast cancer: SWOG S0226." Presented at the 2011 CTRC-AACR San Antonio Breast Cancer Symposium, December 6 - 10, 2011 (presentation S1-1).

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