

Presurgical endocrine therapy less toxic than chemotherapy for ER-positive breast cancer

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Neoadjuvant endocrine therapy - designed to reduce the size of breast tumors before surgical removal - appears to be as effective as neoadjuvant chemotherapy for patients with localized, estrogen-receptor (ER)-positive breast cancer with considerably fewer side effects. The study conducted by a Massachusetts General Hospital (MGH) Cancer Center research team appears in the current print issue of *JAMA Oncology* and was published online earlier this year.

"Estrogen-receptor-positive tumors are generally highly receptive to endocrine therapy with drugs such as tamoxifen and aromatase inhibitors. But while endocrine therapy is the most important component of adjuvant or postsurgical therapy, use of neoadjuvant endocrine therapy has been low in the U.S.," says Aditya Bardia, MD, MPH, of the MGH Cancer Center, an assistant professor of Medicine at Harvard Medical School and senior author of the study. "Since the chemotherapy more commonly used in this situation might not be the best option for patients with these tumors, we conducted a comprehensive, systematic review and meta-analysis to evaluate rigorously the existing scientific evidence."

The authors note that previous studies of neoadjuvant endocrine therapy have been small and as a result had limited statistical power. Their search for prospective, randomized clinical trials of neoadjuvant therapy for ER-positive breast cancer turned up 20 studies involving almost 3,500 patients. In addition to comparing the results of neoadjuvant endocrine and chemotherapy, the researchers also analyzed whether the different types of endocrine therapy - drugs like tamoxifen, which block signaling at the estrogen receptor, or aromatase inhibitors, which inhibit estrogen production - changed treatment results.

Overall, treatment outcomes were similar in patients treated with neoadjuvant chemotherapy and those receiving neoadjuvant endocrine therapy, but patients receiving chemotherapy had significantly greater toxic side effects. Comparing the results of different endocrine therapies revealed that neoadjuvant treatment with aromatase inhibitors was significantly more effective than treatment with tamoxifen-like drugs.

"Endocrine therapy is an approved option for neoadjuvant treatment of localized estrogenreceptor-positive breast cancer, so there's no reason our findings cannot be applied to treatment right now," says Laura Spring, MD, the lead author and a senior oncology fellow at the MGH Cancer Center. "With the spurt in development of new targeted therapies, particularly CDK4/6 inhibitors, more research is needed to look at combining endocrine therapy with those drugs for neoadjuvant treatment." Such a study combining endocrine therapy with a CDK 4/6 inhibitor is currently underway at the MGH and other sites, and information about the trial is available at https://www.clinicaltrials.gov/ct2/show/NCT0271272 3.

More information: Laura M. Spring et al, Neoadjuvant Endocrine Therapy for Estrogen Receptor–Positive Breast Cancer, *JAMA Oncology* (2016). DOI: 10.1001/jamaoncol.2016.1897

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