Nonhormonal treatment regimens improve survival in patients with metastatic breast cancer

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Nonhormonal treatment regimens, including anthracycline-based regimens and taxanes, have improved overall survival in women with advanced (metastatic or recurrent inoperable) breast cancer over the last 35 years, according to a systematic review published December 9 in the *Journal of the National Cancer Institute.*

Numerous regimens have been tested in advanced breast cancer. However, each of the trials has compared only a few regimens, making it difficult for researchers and clinicians to know the relative merit of the individual regimens.

To learn how regimens compare with one another, John P. A. Ioannidis, M.D., of the University of Ioannina School of Medicine in Greece and colleagues performed a meta-analysis of 128 clinical trials that included 148 comparisons between regimens and that enrolled 26,031 women with advanced breast cancer. The investigators used single-agent chemotherapy with old non-anthracycline drugs as the baseline for comparison within their meta-analysis.

The use of anthracycline regimens led to a 22□□ percent relative risk reduction in overall mortality as compared with older single agent chemotherapy. Single drug taxane treatment led to a similar relative risk reduction of 33 percent, while the combination of a taxane with capecitabine or gemcitabine led to a 51 percent relative risk reduction

over the single agent chemotherapy. Most of the regimens appeared to have similar efficacy when used in women who had not been previously treated and in women who had had prior therapy.

"Our meta-analysis quantifies the progress achieved in the treatment of advanced breast cancer with nonhormonal systemic treatment in the last 35 years. Several regimens have shown effectiveness, and for some of them, the treatment effects are practically indistinguishable in magnitude," the authors write. "Given that subsequent lines of treatment can confer similar relative benefits as the first-line setting, one can exploit the survival benefits conferred by several effective regimens used in sequential fashion."

In an accompanying editorial, Philippe Bedard, M.D., and Martine Piccart-Gebhart, M.D., Ph.D., of the Jules Bordet Institute in Brussels, Belgium, note that there has been no consensus regarding the best dosage, timing, sequence or combination of therapies for the treatment of metastatic breast cancer because standard comparators have not been available. Therefore, the work of Ioannidis and colleagues is important.

Given the investigators' finding that many of the regimens have similar relative effectiveness in previously-untreated and -treated patients, no clear order of use appears from the meta-analysis. Other considerations, such as toxicity, will continue to help drive the choice of regimen for individual therapy, the editorialists argue.

"Although this network meta-analysis is unlikely to alter routine clinical practice, it provides a solid evidence-based foundation to support the observation that the survival of women diagnosed with advanced breast cancer has improved because of more active systemic chemotherapy and targeted therapy," the editorialists write. "This should provide hope to patients, investigators, industrial sponsors, and regulatory agencies alike that well-designed clinical trials with novel systemic therapies can

further alter the natural history of this devastating disease."

Source: Journal of the National Cancer Institute

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