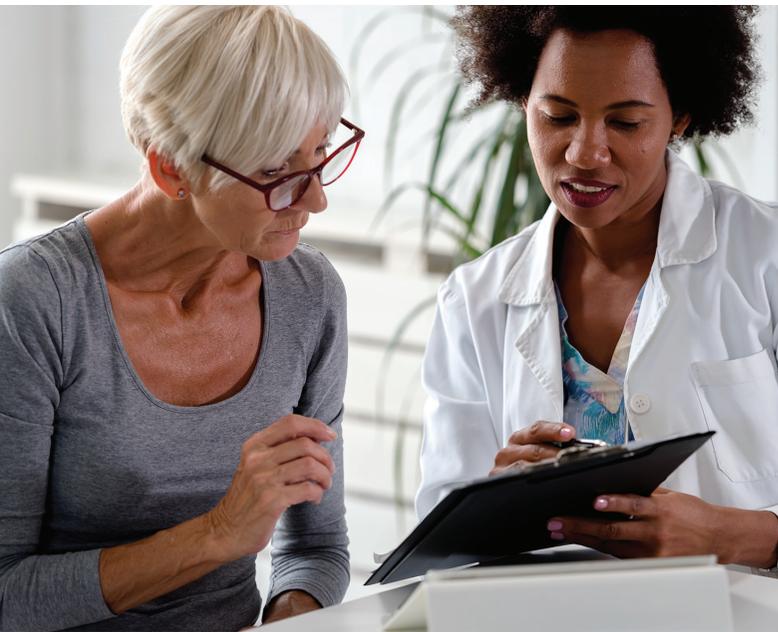


# CancerScope

Oncology Issues in FOCUS | BY CARRIE PRINTZ



## Some Patients With Postmenopausal Breast Cancer Can Avoid Adjuvant Chemotherapy

Data indicate that some postmenopausal women with breast cancer can safely skip adjuvant chemotherapy

**A** greater number of patients with breast cancer can safely avoid having to receive adjuvant chemotherapy according to median follow-up results from the Rx for Positive Node, Endocrine Responsive Breast Cancer (RxPONDER) study presented at the virtual 2020 San Antonio Breast Cancer Symposium.

Findings show that postmenopausal women who have stage II to III, HR-positive, HER2-negative breast cancer with 1 to 3 positive axillary lymph nodes and an Oncotype DX recurrence score of 25 or lower can avoid adjuvant chemotherapy. Premenopausal women with these same criteria should still receive adjuvant chemotherapy, however, because the chemotherapy improved the invasive disease-free survival rate by 5% in this group, researchers say.

“Prior to this, we didn’t have a high-quality, randomized trial on what we should do for patients with positive lymph nodes,” says Debu Tripathy, MD, chair of the Department of Breast Medical Oncology at The University of Texas MD Anderson Cancer Center in Houston. “When historically we

would have recommended chemotherapy for these patients, this study identified a group of them who do not need it.”

The study results mean that thousands of women can be spared the physical and financial toxicities of chemotherapy. In addition, the results provide more guidance to physicians as to which patients still need to receive chemotherapy, says the study’s lead author Kevin Kalinsky, MD, MS, director of the Glenn Family Breast Center at the Winship Cancer Institute of Emory University in Atlanta, Georgia.

“Increasingly, in cancer care we’re trying to move beyond a one-size-fits-all approach, and we had already seen in previous studies of node-negative breast cancer which patients needed chemotherapy,” he says, adding that the results from this third interim analysis of the study were so important that the National Cancer Institute recommended releasing them.

### Comparing Patient Disease-Free Survival Rates

RxPONDER, which was designed and run by the SWOG Cancer Research Network with support from the National Cancer Institute, followed 5083 patients with stage II to III breast cancer involving 1 to 3 axillary lymph nodes whose tissue had a recurrence score of 25 or lower. The international trial was conducted at 632 sites in 9 countries: the United States, Canada, Mexico, Colombia, Ireland, France, Spain, Korea, and Saudi Arabia. Participants were randomly assigned (1:1) to either endocrine therapy alone or endocrine therapy plus chemotherapy. Approximately two-thirds of the patients were postmenopausal. All patients also were receiving endocrine therapy.

Oncotype DX recurrence scores can range from 0 to 100. The genome-based, individualized risk assessment evaluates 16 cancer-related genes in early-stage breast cancer to determine recurrence risk. When evaluating the entire study population of both premenopausal and postmenopausal patients, researchers found no chemotherapy benefit for women with recurrence scores between 0 and 25; they did, however, find a significant association between chemotherapy benefit and menopausal status. Results were the same regardless of the surgery type or whether patients had a single lymph node biopsy or full lymph node dissection. The recurrence score was independently prognostic even when the size, grade, and number of lymph nodes were taken into account, Dr. Kalinsky notes.

In a comparison of postmenopausal patients who did and did not receive adjuvant chemotherapy, the invasive disease-free survival rates were nearly the same: 91.6% and 91.9%, respectively. Among the premenopausal patients, however, the 5-year invasive disease-free survival rate was 94.2% for those who received chemotherapy and 89% for those who did not.

Researchers say that they are reporting on their data at 53.7% of expected invasive disease-free survival events. They



will continue their follow-up of these patients for a total of 15 years and will perform analyses of additional subsets of data as well as quality-of-life and cost-effectiveness analyses.

“This is a common situation that we see all the time in clinic, and these were eagerly anticipated results,” Dr. Kalinsky says. “It’s helping us inform the conversations we’re having with patients.”

“We’d like to maximize our ability to identify patients who do not need chemotherapy,” Dr. Tripathy adds. “There’s no perfect system. We may miss some patients who may need it or treat some who don’t, but we want to be as accurate as possible so that the total number of patients we’re seeing are not recurring and are avoiding chemotherapy when it isn’t needed.”

RxPONDER comes on the heels of the Trial Assigning Individualized Options for Treatment (Rx) (TAILORx) clinical trial, which evaluated whether patients with HR-positive, HER2-negative breast cancer who have lymph node-negative disease should receive chemotherapy on the basis of their Oncotype DX recurrence score. This trial found that patients with a recurrence score of 25 or lower did not benefit from chemotherapy, whereas those with a score of 26 or higher did.<sup>1</sup> A subset analysis of TAILORx patients aged 50 years or younger with recurrence scores of 16 to 25, however, showed that this group did benefit from chemotherapy.

### The Value of Ovarian Function Suppression

One of the main unanswered issues emerging from these studies is whether the benefit from chemotherapy in premenopausal patients occurred because chemotherapy put them into early menopause (thus reducing their estrogen levels) or because it halted the cancer’s progression in other ways.

“We haven’t distinguished between those two possibilities in these studies,” Dr. Tripathy says. “It would have been better if we had known ahead of time that the best standard of care for high-

risk patients is to suppress their ovaries for 5 years with monthly injections, but we weren’t doing that at the time these trials were run.”

Clinicians learned about the value of suppressing ovarian function in this patient population through the Suppression of Ovarian Function Trial (SOFT) and the Tamoxifen and Exemestane Trial (TEXT).<sup>2</sup> These trials showed that among premenopausal women with breast cancer, adding ovarian suppression to tamoxifen resulted in significantly higher 8-year rates of both disease-free and overall survival than treatment with tamoxifen alone. Furthermore, using the aromatase inhibitor exemestane plus ovarian suppression resulted in even higher rates of reduced recurrence.<sup>3</sup>

Both Dr. Tripathy and Dr. Kalinsky say that answering the question of whether ovarian suppression would be as beneficial as chemotherapy would be important for future studies to consider.

“One of the things for us to think about as a community is doing a prospective study where we’re randomizing patients to get chemotherapy followed by endocrine therapy versus endocrine therapy with ovarian function suppression,” says Dr. Kalinsky. “Hopefully, it will be designed in the future.”

Meanwhile, Dr. Tripathy would like to see a study evaluating higher risk patients with 4 to 10 positive lymph nodes. “While it isn’t as common, there still may be some of these patients who may not need chemotherapy,” he says.

### References

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DOI: 10.1002/cncr.33635

## Female Breast Cancer Most Commonly Diagnosed Cancer Globally

**F**emale breast cancer has surpassed lung cancer as the most commonly diagnosed cancer in the world according to a collaborative report from the American Cancer Society (ACS) and the International Agency for Research on Cancer.

The report, titled “Global Cancer Statistics 2020” and published in *CA: A Cancer Journal for Clinicians*, outlines cancer incidence and mortality at the global level according to sex, geography, and levels of social and economic development. It also discusses risk factors and prospects for prevention in each of the 10 major cancer types, which together result in more than 60% of new cancer cases and more than 70% of cancer deaths.<sup>1</sup>

An estimated 19.3 million new cancer cases and almost 10 million cancer deaths occurred in 2020, and female breast cancer, accounting for 2.3 million cases (11.7%), was the most commonly diagnosed cancer according to the report. It was followed by lung cancer (11.4%), colorectal cancer (10%), prostate cancer (7.3%), and stomach cancer (5.6%).

The incidence of breast cancer is increasing in countries

where rates have been historically low. The authors say that dramatic changes in lifestyle and built environments have influenced risk factors, such as excess body weight, physical inactivity, alcohol consumption, postponement of childbearing, fewer childbirths, and less breastfeeding.

Breast cancer death rates were higher in transitioning countries (those with low or medium Human Development Index scores) in comparison with transitioned countries (those with high or very high Human Development Index scores) at 15 and 12.8 per 100,000, respectively, even though transitioning countries had substantially lower incidence rates than transitioned countries at 29.7 and 55.9 cases per 100,000, respectively. The reason for the higher death rates in transitioning countries is that breast cancer is detected at a later stage in these areas. As a result, the authors say that efforts to promote early detection and timely and appropriate treatment are urgently needed in transitioning countries. Specifically, evidence-based and resource-stratified guidelines should be implemented, says Hyuna Sung, PhD, lead