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Deciding When Neoadjuvant Endocrine Therapy is OK for Patients with Operable Breast Cancer

BY ROBERT H. CARLSON

MIAMI BEACH—The indications for neoadjuvant endocrine therapy in patients with operable breast cancer have been the subject of much debate. "There is some reluctance in the U.S. to embrace this concept as wholeheartedly as people in other parts of the world," said William Gradishar, MD, Professor of Breast Oncology and Director of the Center for Women's Cancer Care at Lurie Comprehensive Cancer Center at Northwestern University Feinberg School of Medicine, speaking here at the Miami Breast Cancer Symposium.

He said that neoadjuvant endocrine therapy would be suitable for patients with estrogen receptor (ER)-rich cancers (Allred 7+8) and older postmenopausal women, as well as younger women with significant morbidities.

In the U.S., the use of neoadjuvant, or primary systemic, therapy has largely been limited to chemotherapy alone, or more recently to anti-HER2 therapy combined with chemotherapy for tumors that overexpress HER2 and are not candidates for immediate surgery, he said.

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Endocrine agents are the less commonly used as a systemic approach for patients with ER-positive breast cancer, an approach that has been used mainly for patients who are not considered candidates for chemotherapy based on age or comorbidities.

Neoadjuvant endocrine therapy has largely been limited to this medically infirm patient population, but more recent data have begun to broaden the patient population who are appropriate for this approach, he said.

"The concept of neoadjuvant endocrine therapy may be forced upon us as endocrine therapies are being partnered with some of the new targeted therapies, such as mTOR inhibitors and PI3-kinase inhibitors."

Pathologic CR May Not Be Holy Grail

Gradishar said the notion that a pathologic complete response to neoadjuvant therapy may confer long-term benefit is the "Holy Grail" upon which every drug approval has been linked.

"A concept we often grab onto in the U.S. is that we want to make the tumor shrink, we all want to make it go away, but it is not fully appreciated that pCR is not as important in predicting the outcome of ER-positive cancers," he said, adding, though, that studies nonetheless routinely show that a pCR is better than not having one.

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standard histopathologic measurement, as well as other limitations, Anderson cautioned, noting that the study data show a 26 percent reduction in the number of patients who need a reexcision.

"However, the control group had a 41 percent reexcision rate, so that 26 percent reduction took them down to 30 percent. I think most of us would consider those numbers terribly high. In our center our reexcision rate is around 16 to 18 percent. So the benefit in that setting might be a little different than one would see."

Biology Counts

Emerging evidence suggests that the most important predictor of local recurrence may in fact be biological, Anderson said. Local-regional recurrence correlates with biological factors, but more extensive surgery does not overcome aggressive biology: "Aggressive surgery does not overcome aggressive biology. What is really needed are better drug treatments to manage this," he said.

And adjuvant radiotherapy and systemic treatments have local as well as distant influence on recurrence risk. "The 'wider is better' paradigm for surgical margins may be incorrect, at least in the era of effective adjuvant therapies."