A new study has found that patients with breast cancer who have higher expectations of adverse events from endocrine therapy actually do experience more side effects than those women with a more optimistic pretreatment outlook (Ann Oncol. 2016;27:1909–1915). Side effects are a major cause of nonadherence to medications and nonadherence is a well-documented problem, with multiple prior studies of endocrine therapy for breast cancer reporting nonadherence rates of up to 55%.

In the current study, researchers set out to examine the impact of side-effect expectations on actual side effects, quality of life, and adherence in a 2-year prospective study of patients with breast cancer initiating adjuvant endocrine therapy.

“It is important for clinicians to keep in mind that patients’ individual expectations about endocrine therapy are likely to contribute to the treatments’ clinical outcome in terms of health-related quality of life, side effects, even adherence and thus survival,” says Yvonne Nestoriuc, PhD, lead author and professor in the department of psychosomatic medicine and psychotherapy at the University Medical Center Hamburg-Eppendorf in Germany. “This mental image consists of individual expectations about the potential benefit and harms of this medication and it is directly influenced by the information patients are receiving, first and foremost by their treating clinicians, but of course also by their friends and family, fellow patients, and the media.”

The Study
Dr. Nestoriuc and her colleagues recruited 111 patients with hormone receptor–positive breast cancer who were undergoing surgery and for whom adjuvant endocrine therapy was recommended at a university breast cancer center from January 2011 to March 2012. All patients took part in an educational session at which an informational leaflet was distributed and a discussion explaining the possible side effects of endocrine therapy followed. Side effects, baseline symptoms, side-effect expectations, health-related quality of life, and adherence were assessed using validated scoring methods at baseline (111 patients), 3 months (107 patients), and 24 months (88 patients).

At baseline, 8% of patients expected no side effects, 63% expected mild side effects, and 30% expected moderate to severe side effects. Patients expecting moderate to severe problems were significantly more likely to drop out of the study. Baseline-controlled rates for side effects at 24 months were highest for arthralgia, weight gain, and myalgia at 71%, 53%, and 51%, respectively.

The side effects at 3 months significantly correlated with baseline expectations (P < .001). Side effects at 24 months also correlated with baseline expectations (P = .001). No associations with other clinical variables such as staging, type of medication, or receipt of chemotherapy were observed. In multivariate models taking into consideration medical and psychological factors, pretreatment expectations continued to significantly predict actual side effects. The relative risk of side effects for those individuals with highly negative outlooks at baseline versus patients with low negative expectations was 1.672 at 3 months and 1.833 at 24 months.

KEY POINTS
- A higher expectation of side effects from adjuvant endocrine therapy increased the risk of actual side effects experienced.
- Adherence was worse in patients with higher expectations of side effects from adjuvant endocrine therapy, and health-related quality of life was lower.
Adherence at 24 months significantly correlated with side effects at 3 months and with baseline side effect expectations. Furthermore, a higher expectation of side effects also predicted lower health-related quality of life.

This research adds to the body of evidence demonstrating that words and labels matter when communicating with patients, says William Breitbart, MD, chief of the psychiatry service at Memorial Sloan Kettering Cancer Center in New York City. “For example, in a prior study of postsurgical pain, patients who were asked if they had any ‘expected discomfort’ were less likely to report pain and less likely to take pain medications than patients who were repeatedly asked to rate their ‘pain,’” says Dr. Breitbart. “Labeling a sensation as pain as opposed to discomfort, which lead to a different interpretation of the symptom and different behaviors,” he says.

Implications
Former US Surgeon General C. Everett Koop once famously said “drugs don’t work in patients who don’t take them.” The authors of the current study note that they hope that understanding patients’ expectations of side effects more fully will help to form new clinical strategies that may help to lessen side effects and improve adherence, which may improve breast cancer outcomes.

Prior studies from different researchers have shown that nonadherence to adjuvant endocrine therapy predicts lower survival rates. “When prescribing endocrine therapy, clinicians should aim to give [patients] at least as much encouraging information about the positive effects of a treatment and its mechanism of action as they give information about potential side effects,” says Dr. Nestoriuc. “Furthermore, clinicians can point out the importance of patients’ own perceptions of a medication to help them seek positive information about that treatment as opposed to worst case scenarios (eg, when they are looking for information on the Internet).” Dr. Nestoriuc says she also believes that the findings may be generalized to other patients receiving medications for chronic conditions.

The authors of the study are applying their results to a new trial that is testing clinical strategies. “We are currently carrying out a randomized controlled trial in 3 certified breast care centers in Germany to see whether strategies for improving women’s expectations are effective,” says Dr. Nestoriuc.

“Our side effects prevention training consists of [3 counselling sessions] by psychologists [that take place] just before the start of treatment. It includes information on treatment that highlights its benefits, mechanisms of action, and potential side effects, that also explains about the possible effects of expectations (explicitly the nocebo effect), and that gives patients individual strategies for coping with side effects.”

“At the end of the training, each woman has developed her own set of strategies to cope with the potential side effects she fears the most,” Dr. Nestoriuc adds. “Regarding the positive effects of treatment, an imagination exercise is carried out in which patients are invited to visualize how their medication is protecting them from recurring tumors or metastases. It is fascinating how this leads some patients to rename their medication (consistent with their mental image), such as umbrella instead of tamoxifen.”

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